AN INVESTIGATION ON THE INCIDENCE AND PREVALENCE OF DRUG RELATED OUTCOMES IN HYPERTENSIVE PATIENTS ON ACE INHIBITORS

A Dissertation submitted to

THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY
Chennai-600032

In partial fulfillment of the requirements for the award of degree of

MASTER OF PHARMACY
IN
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Submitted by

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This is to certify that the dissertation entitled **"An Investigation on the Incidence and Prevalence of Drug related outcomes in Hypertensive Patients on ACE Inhibitors"** submitted to The Tamilnadu Dr. M.G.R Medical University, Chennai, is a bonafide project work of **NITHYA R. (Reg No: 261540453),** carried out in the Department of Pharmacy Practice, Swamy Vivekanandha College of Pharmacy, Tiruchengode in partial fulfillment for the degree of Master of Pharmacy under the guidance of **Mr. JOSEPH STALIN D, M. Pharm.,** Assistant Professor, Department of Pharmacy Practice during the academic year 2016-2017.

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This work is original and has not been submitted earlier for the award of any other degree or diploma in this or any other university.

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EVALUATION CERTIFICATE

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ABBREVIATIONS

ACE	-	Angiotensin Converting Enzyme
ACS	-	Acute Coronary Syndrome
ADR	-	Adverse Drug Reactions
ALP	-	Alkaline Phosphatase
ALT	-	Alanine Aminotransferase
ARB	-	Angiotensin Receptor Blocker
AST	-	Aspartate Amino Transferase
BP	-	Blood Pressure
CAD	-	Coronary Artery Disease
CCB	-	Calcium Channel Blockers
CI	-	Confident Interval
CKD	-	Chronic Kidney Disease
DBP	-	Diastolic Blood Pressure
DILI	-	Drug Induced Liver Disease
ESR	-	Erythrocyte Sedimentation Rate
HF	-	Heart Failure
IKES	-	Isokinetic Knee Extensor Strength
IP	-	In Patient
MI	-	Myocardial Infarction
NDP	-	Nedaplatin

NHANES	-	National Health and Nutrition Examination Survey
NSTEMI	-	Non ST Elevated Myocardial Infarction.
OPD	-	Out Patient Department
OR	-	Odds Ratio
PEM	-	Protein Energy Malnutrition
PTCA	-	Percutaneous Coronary Angiogram
RAAS	-	Renin Angiotensin Aldosterone System
RR	-	Respiratory Rate
SBP	-	Systolic Blood Pressure
SUA	-	Serum Uric Acid

1. INTRODUCTION

ACE Inhibitors are the first class of drugs that represents antihypertensive agents which were designed and developed with the basis of a well–defined pathophysiological axis of arterial hypertension, a vascular disorder which is now becoming one of the major causes of morbidity and mortality, not only in developed societies but also in the highly populated developing countries.[1]

Since their initial development in the 1970s as a therapy for hypertension, ACE inhibitors have become established as cornerstones in the treatment of hypertension, heart failure and myocardial infarction (MI).[2]

They are also considered as the first-line choice of treatment of hypertension in younger patients, and a second-line choice in all patient groups.[3]

1.1 MECHANISM OF ACTION

These agents inhibit angiotensin-converting enzyme (ACE), thus preventing conversion of angiotensin I to angiotensin II, which is a potent vasoconstrictor and stimulator of aldosterone secretion (aldosterone suppression reduces sodium and water retention). ACE inhibitors also prevent the breakdown of bradykinin (a potent vasodilator). The net result is vasodilatation, decreased peripheral vascular resistance, decreased blood pressure, increased cardiac output, and a relative increase in renal, cerebral and coronary bloodflow.[4]

1.2 INDICATIONS

The main indications of ACE inhibitors are as follows

1.2.1 Hypertension

An ACE inhibitor may be the most common appropriate initial drug for hypertension in younger patients; some patients aged over 55 years, and those with primary aldosteronism respond less well. ACE inhibitors are particularly indicated for hypertension in patients with type 1 diabetes with nephropathy. They may reduce blood pressure very rapidly in some patients particularly in those receiving diuretic therapy; the first dose should preferably be given at bed time.

1.2.2 Heart failure

ACE Inhibitors are used in all grades of heart failure, usually combined with a beta blocker .potassium supplements and potassium sparing diuretics.

However, a low dose of spironolactone may be beneficial in severe heart failure and can be used along with an ACE inhibitor provided serum potassium is monitored carefully Profound first-dose hypotension may occur when ACE inhibitors are introduced to patients with heart failure who are already taking a high dose of loop diuretic (e.g. furosemide 80mg daily or more).Temporary withdrawal of loop diuretics reduces the risk, but may cause severe rebound pulmonary oedema.

Therefore for patients on high doses of loop diuretics, the ACE inhibitor may need to initiated under specialist supervision, An ACE inhibitor can be initiated in patients who are receiving a low dose of a diuretic or who are not otherwise at risk of serious hypotension; nevertheless, care is required and a very low dose of the ACE inhibitor is given initially.

1.2.3 Diabetic Nephropathy

ACE inhibitors are particularly useful for people with diabetic nephropathy because they significantly decrease the amount of protein in the urine and can also prevent or slow the progression of diabetes-related kidney disease. The kidney benefits of ACE inhibitors are so robust that the healthcare providers sometimes prescribe them for people with diabetic nephropathy who have normal blood pressure.

1.2.4Prophylaxis of Cardiovascular Events

ACE inhibitors are used in the early and long-term management of patients who had a myocardial infarction; ACE inhibitors may also have a role in preventing cardiovascular events.

ACE inhibitors should be initiated under specialist supervision and with careful clinical monitoring in those with severe heart failure or in those:

- with hypovolaemia;
- with hyponatremia (plasma-sodium concentration below 130mmol/litre);
- with hypotension (systolic blood pressure below 90mmHg);
- with unstable heart failure;
- receiving high dose vasodilator therapy;
- known renovascular disease.[5]

1.3CLASSIFICATION

ACE Inhibitors can be divided into three groups based on their molecular structure:

- **Sulfhydryl-containing agents:**
  - Captopril , the first ACE inhibitor
- **Dicarboxylate-containing agents:**
  - Enalapril
  - Ramipril
  - Quinapril
  - Perindopril
  - Lisinopril
  - Benazepril
- **Phosphonate-containing agents:**
  - Fosinopril

Based on the effectiveness and drug choice depending on the indications, ACE Inhibitors can be classified as:

- For high blood pressure: Benazepril, Enalapril, and Lisinopril
- For heart failure: Captopril, and Enalapril
- After a heart attack: Lisinopril
- For diabetics: Ramipril
- For people with kidney disease: Benazepril, and Ramipril.[6]

1.4PHARMACOKINETICS

1.4.1 Captopril

Onset 30 minutes, duration 8 to 12 hours, and 70% absorbed. Peak concentrations about 1 hour; 25% protein bound, volume of distribution 0.7 L/kg, 50% hepatic metabolism, renal elimination, and half-life 1.9 hours.

1.4.2 Enalapril

Onset 1 to 4 hours, duration 12 to 24 hours, and 60% absorbed. Peak concentrations 1 hour, 50% protein bound, active hepatic metabolite (enalaprilat) which is renally eliminated. Half-life: enalapril 1.3 hours; enalaprilat 11 hours.

1.4.3 Lisinopril

Onset 1 hour, duration 24 hours, and about 25% absorbed. Peak concentration 6 to 8 hours, minimal protein binding, volume of distribution 124 litres, elimination: mostly faecal followed by renal and half-life 12 hours.

1.4.4 Perindopril

Onset 1.5 hours, duration 24 hours, 20% to 30% absorbed, and 60% protein bound. Volume of distribution 0.33 L/kg, extensive hepatic metabolism, 75% renal and 25% faecal elimination of metabolites. Half-life 1 hour.[7]

1.5CONTRAINDICATIONS

ACE inhibitors are contraindicated in patients with hypersensitivity to ACE inhibitors. (Including angioedema)

1.5.1 Hepatic Impairment

Use of prodrugs such as cilazapril, enalapril, fosinopril, imidapril, moexipril, Perindopril, quinapril, ramipril and trandolapril requires close monitoring in patients with impaired liver function.

1.5.2 Renal Impairment

ACE inhibitors should be used with caution and the response monitored, hyperkalemia and other side effects are more common; the dose may be needed to be reduced.

1.5.3 Pregnancy

ACE inhibitors should be avoided in pregnancy unless essential. They may adversely affect foetal and neonatal blood pressure control and renal function; skull defects and olihohydramnios have also been reported.

1.5.4 Breast Feeding

Information on the use of ACE inhibitors in breast feeding is limited.

Cilazapril,Fosinopril, Imidapril, Moexipril, Perindopril, Ramipril and Tranolapril are not recommended; alternative treatment options, with better established safety information during breast-feeding are available. Captopril, Enalapril and Quinapril should be avoided in the first few weeks after delivery, particularly in preterm infants, due to the risk profound neonatal hypotension; ifessential, they may be used in mothers breastfeeding older infants -the infant's blood pressure should be monitored.[8]

1.6DRUG INTERACTION

1.6.1 Albumin

Profound hypotension developed in a patient on captopril after receiving 4% albumin. The albumin contained 10 IU/mL of prekallikrein activating factor (PKA) PKA activates bradykinin while ACE inhibitors block the biodegradation of bradykinin, potentially causing persistent hypotension in this setting.

1.6.2 Allopurinol

Concomitant use of captopril and allopurinol has rarely been associated with a serum sickness or Stevens-Johnson syndrome

1.6.3 Antihyperglycemic Agents

Hypoglycaemia has been reported with simultaneous use of ACE inhibitors and insulin or oral hypoglycemic agents.

1.6.4 Cyclosporine

The combination of cyclosporine and ACE inhibitors may rarely cause acute renal failure.

1.6.5 Diuretics

The combination of ACE inhibitors and potassium-sparing diuretics may cause hyperkalemia.

1.6.6 Hemodialyzer Membranes

Several cases of life-threatening anaphylactic reactions have been reported in patients receiving ACE inhibitors and hemodialysis with a polyacrylonitrile membrane dialyzer (AN69).

1.6.7 Nonsteroidal Anti-inflammatory Drugs

The combination of NSAIDs and ACE inhibitors may cause renal insufficiency

1.6.8 Wasp Venom

Anaphylactic reactions have been reported after co-administration of enalapril and wasp venom, presumably due to amplification of the inflammatory response induced by the kallikrein-kinin system.[8]

1.7 ADVERSE EFFECTS

- ACE Inhibitors can cause profound hypotension and renal impairment and a persistent dry cough
- They can also cause angioedema (onset may be delayed; higher incidence reported in Afro-Caribbean patients), rash (which may be associated with pruritisand urticaria), pancreatitis
- Upper respiratory-tract symptoms such as sinusitis, rhinitis and sore throat
- Gastrointestinal effects reported nausea, vomiting, dyspepsia,diarrhoea, constipation and abdominal pain
- Altered liver function tests, cholestatic jaundice,hepatitis, fulminant hepatic necrosis and hepatic failure have been reported- discontinue if marked elevation of hepatic enzymes or jaundice
- Hyperuricaemia
- Hyperkalemia
- Hypoglycaemia
- Blood disorders such as thrombocytopenia, leucopenia, neutropenia and haemolytic anaemia have also been reported.

Other reported adverse effects include

- Headache
- Dizziness
- Fatigue
- Malaise
- Taste disturbance
- Paraesthesia
- Bronchospasm
- Fever
- Serositis
- Vasculitis
- Myalgia
- Arthralgia
- Raised erythrocyte sedimentation rate (ESR)
- Eosinophilia
- Leucocytosis
- Photosensitivity.

1.8TOXICOLOGY

The toxic effect of an ACE inhibitor is an extension of its pharmacologic effect. The elevation in bradykinin concentration appears to be the primary cause of both ACE inhibitor-induced angioedema and cough. ACE inhibitors may also inhibit the metabolism of enkephalins and potentiate their opioid effect, which includes lowering blood pressure.

1.9COMBINATION PRODUCTS

Products incorporating an ACE inhibitor with a thiazide diuretic or a calcium-channel blocker are available for the management of hypertension. Use of these combination products should be reserved for patients whose blood pressure has not responded adequately to a single antihypertensive drug and who have been stabilised on the individual components in the same proportions.[8, 9]

1.10CAPTOPRIL

Dose

- Initial dosage: 25 mg orally 2 or 3 times daily; may increase to 50 mg orally 2 or 3 times daily after 1 to 2 weeks; Maintenance dosage: 25 to 150 mg orally 2 or 3 times daily
- Maximum dosage: 450 mg/day

Contraindications:

- Angioedema history related to prior therapy with an ACE inhibitor.
- Hypersensitivity to captopril or to any other ACE inhibitor.
- Coadministration with aliskiren in patients with diabetes
- Concomitant neprilysin inhibitors (eg,sacubitril) or within 36 hours of switching to or fromsacubitril/valsartan[10]

Adverse Effects

Angina pectoris

- Incidence: 0.2% to 0.3%
- Angina pectoris has been reported as occurring in 0.2% to 0.3% of patients

receiving captopril in clinical trials. Increased lactate production which may indicate myocardial ischemia and may exacerbate angina has been reported, with episodes of angina leading to drug withdrawal. In contrast, captopril may enhance regional coronary blood flow and has been used to treat angina pectoris.

Chest pain

Chest pain has been observed in approximately 1 in 100 patients receiving captopril in clinical trials.

Flushing

- Incidence:0.2% to 0.5%
- Flushing or pallor has been reported as occurring in 2 to 5 of 1000

  Patients receiving captopril

Hypotension

Although excessive hypotension was rare in patients treated with captopril for hypertension, it is a possibility in volume or salt depleted patients, patients with heart failure, or patients undergoing renal dialysis.

Gastrointestinal Effects

Diarrhoea

- Incidence: 0.5% to 2%

Hepatic Effects

Hepatotoxicity

Immunologic Effects

- Anaphylactoid reaction
- Renal effects

- Acute renal failure
- Hyperuricaemia
- Glomerulonephritis
- Nephrotic syndrome
- Nephrotoxicity
- Proteinuria

Reproductive Effects

- Erectile dysfunction

Respiratory Effects

- Bronchospasm
- Cough

Other

- Angioedema. [11]

1.11ENALAPRIL

Dose

- Initial dosage: 5 mg orally once daily
- Maximum dosage: 40 mg orally daily; may divide dose and administer twice daily.
- Usual dosage range: 10 to 40 mg/day in single or divided doses.
- Concomitant medication: Initiate at 2.5 mg/day if co- administered with a low-dose diuretic.[12]

Indications

Enalapril maleate oral tablets and oral solutions are indicated for the treatment of hypertension in adults and children older than 1 month.

Contraindications

- Concomitant aliskiren use in patients with diabetes.
- Concomitant neprilysin inhibitors (e.g. sacubitril) or within 36 hours of switching to or from sacubitril/valsartan
- Hereditary or idiopathic angioedema
- History of angioedema related to prior therapy with an ACE Inhibitor
- Hypersensitivity to enalapril or an ACE inhibitor

Adverse effects

Common or very common

- Bronchitis
- Syncope
- Hyperuricaemia

Uncommon

- Angina
- Anxiety
- Arrhythmias
- Chest pain
- Decreased libido
- Flushing
- Impotence.[13]

1.12RAMIPRIL

Dose

The recommended initial dose of ramipril for the treatment of hypertension is 2.5 mg orally once daily in patients not receiving a diuretic, adjusted according to response. The usual maintenance dose is 2.5 to 20 mg daily, which may be administered as a single dose or in 2 divided doses. If diuretic therapy is used concurrently, a decrease in the starting dose of ramipril may be required.[14]

Contraindications

- Concomitant use with a neprilysin inhibitor or use within 36 hours of switching to or from sacubitril/valsartan, a neprilysin inhibitor,
- Concomitant aliskiren use in patients with diabetes
- History of angioedema related to prior therapy with an ACE inhibitor,
- Hypersensitivity to ramipril, any component of this product, or to anotherACE inhibitor.

Adverse Effects

Common or very common

- Bronchitis
- Dyspnoea.
- Muscle Cramps
- Stomatitis
- Syncope

Uncommon

- Angina
- Anxiety
- Arrhythmias
- Chest Pain
- Decreased Libido
- Depression
- Impotence
- Loss of Appetite
- Myocardial Infarction
- Nervousness
- Palpitations
- Peripheral Oedema
- Sweating
- Tachycardia
- Visual Disturbances

Rare

- Confusion
- Impaired hearing
- Onycholysis
- Tinnitus
- Tremor
- Hyperuricaemia

Frequency Not Known

- Alopecia
- Cerebrovascular Accident
- Erythema Multiforme
- Pemphigoid Exanthema
- Precipitation Or Exacerbation of Raynaud's Syndrome
- Skin Reactions
- Sleep Disturbance
- Stevens-Johnson Syndrome
- Toxic Epidermal Necrolysis.[15]

1.13QUINAPRIL

Dose

Adult

- Initially 10 mg once daily;
- Maintenance 20–40 mg daily in up to 2 divided doses;
- Maximum 80 mg per day.

Elderly

- Initially 2.5 mg once daily;
- Maintenance 20–40 mg daily in up to 2 divided doses;
- Maximum 80 mg per day.

Contraindications

- History of angioedema related to prior therapy with an ACE inhibitor
- Concomitant aliskiren use in patients with diabetes.

- Concomitant use with a neprilysin inhibitor or use within 36 hours of switching to or from sacubitril/valsartan, a neprilysin inhibitor.
- Hypersensitivity to quinapril or any other component of the product.

Adverse Effects

- Impotence
- Asthenia
- Back Pain
- Chest Pain
- Depression
- Flatulence
- Insomnia[16]

1.14FOSINOPRIL SODIUM

Dose

- Initial dose, 10 mg once daily
- Usual dose, 20 and 40 mg daily
- Maximum dose, 80 mg daily

The dose should be adjusted according to the patients response at peak and trough plasma levels, 2 to 6 hours and 24 hours respectively, with divided daily doses indicated if blood pressure control is inadequate with once daily dosing. [17]

Contraindications

Hypersensitivity to fosinopril or other ACE inhibitors

Adverse effects

- Blurred Vision
- Chest Pain or Discomfort
- Chills
- Cold Sweats
- Confusion
- Dizziness, Faintness, or Light Headedness
- Fast, Slow or Irregular Heartbeat
- Pounding or Rapid Pulse
- Sweating
- Unusual Tiredness or Weakness.[18]

1.15PERINDOPRIL

Dose

For the treatment of essential hypertension, the recommended initial dosage of Perindopril erbumine is 4 mg orally once daily. The Perindopril dosage may be titrated up to a maximum of 16 mg daily; however, the usual maintenance dosage is 4 to 8 mg daily given as a single daily dose. The daily Perindopril dose may be also be given in 2 divided doses

Concomitant Use with Diuretic Therapy

In patients already taking diuretic therapy, symptomatic hypotension may occur with the first dose of Perindopril. To minimize this risk, consider reducing the diuretic dose prior to initiating Perindopril.[19]

Contraindications

- Concomitant aliskiren use in diabetic patients
- Hereditary or idiopathic angioedema
- Hypersensitivity (including angioedema) to Perindopril, any component of the Product or other ACE inhibitors.

Adverse Effects

- Asthenia.
- Mood Disturbances.
- Sleep Disturbances. [20]

1.16LISINOPRIL

Dose

- Initial dose,10 mg once daily
- Maintenance dose, 20 mg once daily
- Maximum dose, 80 mg per day

Contraindications

- Concomitant aliskiren use in diabetic patients
- Concomitant neprilysin inhibitors (e.g., sacubitril) or within 36 hours of

Switching to or from sacubitril/valsartan

- Hereditary or idiopathic angioedema
- History of angioedema or hypersensitivity with prior ACE inhibitoruse
- Hypersensitivity to Lisinopril or product components

Adverse effects

Common

- Vertigo
- Asthenia
- Hepatotoxicity
- Cerebrovascular Accident
- Confusion
- Impotence
- Mood Changes
- Myocardial Infarction
- Palpitation
- Sleep Disturbances
- Tachycardia

Rare

- Alopecia
- Dry Mouth
- Gynaecomastia.

Very Rare

- Allergic Alveolitis
- Pemphigus
- Profuse Sweating
- Pulmonary Infiltrates. [21]

1.18 BENAZEPRIL

Dose

Initial, in patients not receiving a diuretic, 10 mg orally once daily; maintenance, 20 to 40 mg orally once daily or in 2 equally divided doses. Divided doses may be more effective for trough or pre-dosing blood pressure than once daily regimens. Doses up to 80 mg/day may increase response but experience is limited. In patients receiving a diuretic, 5 mg orally once daily.[22]

Contraindications

- Angioedema history
- Concomitant aliskiren use in diabetic patients
- Concomitant neprilysin inhibitors (e.g. sacubitril) or within 36 hours of switching to or from sacubitril/valsartan
- Hypersensitivity to benazepril, other ACE inhibitors, or to any component of the product.

Adverse effects

- Blurred vision
- Chest pain or discomfort
- Chills
- Cold sweats
- Confusion
- Dizziness, faintness or light headedness when getting up from a lying or sitting position suddenly
- Fast, slow or irregular heartbeat

- Pounding or rapid pulse
- Sweating
- Unusual tiredness or weakness.[23]

In view of the increasing number of available antihypertensive agents, clinicians are faced with the need to become familiar with the potential drug related outcomes. Unfortunately, adverse antihypertensive drug reactions cannot always be predicted from the pharmacological profile and only prolonged clinical experience will reveal their adverse effects.

In this study we observed the incidence of cardiac events and prevalence of Hyperuricaemia, Liver diseases in Hypertensive patients with ACE inhibitors in a rural population.

2. REVIEW OF LITERATURE

In the year 2017, Aslam Mand his colleagues performed a comparative study on Efficacy and Tolerability of Antihypertensive Drugs in Diabetic and Non diabetic Patients. The study was conducted on 200 hypertensive patients with diabetes and 230 hypertensive patients without (Three hospitals) diabetes. The study was conducted for 4 months. After 4 months; patients were assessed for efficacy by monitoring blood pressure (BP) and tolerability by assessing safety profile on renal function, liver function as well as lipid profile. Adverse effects observed were dry cough, pedal edema, dizziness, muscular cramps, constipation, palpitations, sweating, vertigo, tinnitus, paresthesia, and sexual dysfunction. All classes of antihypertensives were found to control blood pressure significantly in both groups of patients that is diabetic patients with hypertension and non-diabetic patients with hypertension.[24]

In the year 2017, Forner D et al performed a case study on Ramipril-associated cholestasis in the setting of recurrent drug-induced liver injury .Rare reports of ACEI-induced hepatotoxicity have been described, most notably a cholestatic pattern of injury related to captopril. A 67-year-old male presented to the emergency department with a three-week history of jaundice, pruritis and weakness. Eight weeks before, he began taking ramipril and clopidogrel. His past medical history was significant for previous acute cholestatic liver injury approximately 20 years earlier, which was attributed to methimazole. AST, ALT, Serum Bilirubin was abnormal abdominal ultrasound and magnetic resonance cholangiopancreatography showed no bile duct obstruction. This case representsthe first described cross reactivity

between ramipril and methimazole, illustrating the complex and poorly understood nature of DILI. Despite the relatively few instances of ACEI – induced liver hepatotoxicity, consideration should be given to discontinuation of ramipril in situations of unknown liver damage.[25]

In the year 2017, Hallberg Pet al conducted a comparative study on Clinical Factors associated between Patients With Angiotensin-Converting Enzyme Inhibitor-Induced Angioedema and Cough. Data on patients with angioedema or cough inducedby ACE inhibitors were collected from the Swedish database of spontaneously reported ADRs or from collaborating clinicians. Wilcoxon rank sum test, Fisher's exact test, and odds ratios (ORs) with 95% CIs were used to test for between-group differences. Angioedema cases were seen more often in male patients and had longer time to onset and higher doses than those with cough. A multiple model containing the variables smoking, concurrent calcium channels blocker. Smoking, co medication with selective calcium channel blockers, male sex, and longer treatment time were associated with ACE inhibitor-induced angioedema rather treatment, male sex, and time to onset accounted for 26% of the variance between the groups than cough.[26]

In the year 2016, Francesca Viazzi et al conducted a study on Increased Serum Uric Acid Levels blunt the Antihypertensive Efficacy of Lifestyle Modifications in Children at Cardiovascular Risk Preliminary studies in children highlighted uric acid as a potentially modifiable risk factor for the prevention and treatment of hypertension. The risk of hypertension at follow-up was associated with body mass index and systolic blood pressure z-score at baseline and inversely related to delta

body mass index, whereas the risk of showing hypertension ≥99th percentile was more than doubled for each baseline 1 mg/dL increase of serum uric acid .Uric acid is a powerful determinant of blood pressure over time, independent of lifestyle modifications.[27]

In the year 2016, Loprinzi PDand Loenneke JP performed a retrospective study on the effects of antihypertensive medications on physical function. The purpose of this study was to examine whether several antihypertensive medication classes were associated with several measures of physical function in a national sample of middle-to-older age adults. Data from the 2004 -2009 and 2011-2016 NHANES were used. Antihypertensive medication use was assessed from an interviewer, andincluded angiotensin converting enzyme (ACE) inhibitors, peripherally-acting anti adrenergic agents and centrally-acting anti adrenergic agents. Physical function-related parameters included objectively-measured lower extremity isokinetic knee extensor strength (IKES), objectively-measured grip strength, laboratory-assessed walking performance (8 and 20 ft walk tests) and self-reported physical activity engagement. Antihypertensive medication use, particularly ACE inhibitors, is associated with various measures of reduced physical function. Clinicians are encouraged to monitor the long-term mobility function of their patients on antihypertensive medications.[28]

In the year 2016,Imprialos KP et alperformed a prospective study on Current challenges in antihypertensive treatment in the elderly. In the elderly population, elevated BP has been related with increased cardiovascular risk. Trials on this population have shown great benefits for morbidity and mortality from reducing Systolic BP (SBP) levels to less than 150 mmHg. Among the various classes of

drugs, diuretics, calcium channel blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers were proved beneficial in the elderly and are favored as first choices for the management of elderly hypertensive individuals. Given the common coexistence of other co morbidities and polypharmacy. The author also emphasizes that physicians should be careful when initiating or up titrating treatments to avoid potential adverse events or interaction with other drugs or diseases.[29]

In the year 2016, Krogh Nielsen Tand his colleaguesperformed a case study on Life-threatening angio-oedema after the first dose of an ACE inhibitor but not an anaphylactic reaction. A case of a 60-year-old Caucasian woman, with no prior history of swellings, who was admitted to a hospital due to life-threatening angio-oedema. She had, the previous day, been prescribed an ACE inhibitor for her essential hypertension. She had taken one tablet at night-time, and awoke in the morning with a swollen face progressing to involve the tongue and throat within a few hours. On arrival at her doctor's office, her voice had altered. Corticosteroids and antihistamine were administered while awaiting an ambulance. Arriving at the emergency department, she had dyspnoea due to increasingly severe angio-oedema of the upper airways. Neither adrenaline inhalations, intravenously administrated corticosteroids, atropine nor furosemide were effective and the patient soon become bradycardiac. A tracheotomy was performed and the patient was placed on a ventilator. She eventually made a full recovery. It was concluded that she had suffered from life-threatening angio-oedema due to her new medication.[30]

In the year 2016,Simonyi G conducted a subgroup analysis of RAMONA Trial on Benefits of Fixed Dose Combination of Ramipril/Amlodipine in Hypertensive Diabetic Patients. 6423 patients completed the study. Among these patients, 1276 (19.9%) patients suffered from type 2 diabetes mellitus. The mean age of these diabetic patients was 64.2 ± 10.0 years; 707 (55.4%) patients were males. Various fixed dose combinations of ramipril/Amlodipine were well tolerated and no adverse event related to the use of the medicine has appeared. The fixed dose combination of ramipril/Amlodipine was effective in hypertensive diabetic patients who failed to reach target BP previously.[31]

In the year 2015,Rajavel Murugan R. and PadmavathiR. ConductedaStudy of Prevalence of Hyperuricaemia in Hypertension. The study was planned to assess the relation between hyperuricaemia and hypertension. In this study, 85 patients of new onset hypertension and the same number of patients attending NCD clinic were compared. Serum uric acid was measured in all the patients and data compared and analysed by unpaired t test. The mean value for both sexes was above normal and there was significant association between uric acid and hypertension especially in population of more than 45 years.[32]

In the year 2015,Strassen U et al analysed a case series on angiotensin receptor blocker-induced angioedema and its management. The author presented a case series of patients admitted to their hospital due to angioedema induced by an Angiotensin II receptor blocker. The patients were either treated with either icatibant (n = 3) or prednisolone-21-hydrogen succinate/clemastine (n = 5). Both patient groups were compared with an untreated patient cohort (n = 3). All patients were previously diagnosed with essential hypertonic. Icatibant was an effective therapy for

angiotensin II receptor blocker-induced angioedema. Full symptom recovery was achieved after 5 to 7 hours, whereas symptom remission occurred within 27 to 52 and 24 to 54 hours in patients treated with Solu-Decortin prednisolone/clemastine and untreated patients, respectively. Icatibant are a safe and effective substance for the treatment of angiotensin II receptor blocker-induced angioedema. Although the pathophysiology of angiotensin II receptor blocker-induced angioedema remains unclear, it appears to be associated with the bradykinin pathway.[33]

In the year 2015, Fukuda S Conducted a prospective study on frequency and characteristics of cough during ACE inhibitor treatment. Subjects in this study were 176 patients overall (mean age 67 ± 11 years old), 90 men and 86 women. The adverse reaction of cough was observed in 20% of patients, and more frequently in women than in men. However, in 26 of the patients with cough, the cough either resolved naturally or completely disappeared while the treatment continued, after which patients could continue taking the medication. Specifically, ACE inhibitor treatment was eventually discontinued due to cough in 5.1% of patients. Cough occurred less frequently with concomitant calcium antagonists or diuretics than with ACE inhibitor monotherapy. Cough as an adverse reaction occurred at a low frequency when medication was taken at bedtime. They considered a number of measures to counteract cough, then in addition to starting the ACE inhibitor treatment as early as possible, it is important to devise ways for the ACE inhibitor treatment to be continued for as long as possible, through the adept use of these measures.[34]

In the year 2014, Loga Zec S et al performed a prospective study on the Incidence of Antihypertensive Drug-induced Side Effects in Patients with Diabetes Mellitus Type 2 and Hypertension**.** They performed a prospective study of 79 patients with DM type 2 and hypertension, randomly selected by systematic sampling, who were followed over a period of six months. Patients were assessed at baseline and once a month measuring following parameters: types of used antihypertensive drugs and frequency of side effects, the values (mmHg) of systolic (SBP) and diastolic blood pressure (DBP).Out of 79 patients, 60.8%were males and 39.2%were females. The median age in males was 53 years, in females was 53 years (IQR=49 to 56 years). The most common side effect was cough associated with the combination of ACE inhibitor and thiazide diuretics. In patients there were reports of flushing, palpitations, headache, dizziness and leg edema associated with Ca blockers. The most common side effect of antihypertensive treatment was cough associated with the combination of ACE inhibitor and thiazide diuretic.[35]

In the year 2014, Mancia G et al conducted a study on Incidence of adverse events with telmisartan compared with ACE inhibitors. Incidence rates of adverse events for the combined ACE inhibitor treatments and for telmisartan were similar as were the rates of serious adverse events. Patients receiving ACE inhibitors had more cough with telmisartan. Results were similar irrespective of age, gender, or ethnicity. The adverse event of angioedema was observed in four patients receiving ACE inhibitors versus none with telmisartan .There were small, numerical differences in serious adverse events. A total of 107 patients (5.0%) receiving ACE inhibitors and 93 patients (3.6%) receiving telmisartan discontinued treatment because of Adverse

Events. Telmisartan andACEinhibitorsproducedcomparable bloodpressurereductions at marketed doses. Telmisartan and ACE inhibitors are suitable for the prevention of cardiovascular events in high-risk patients, but telmisartan is better tolerated, particularly with regard to cough.[36]

In the year 2014, Brugts JJand his colleagues conducted a prospective study on the incidence and clinical predictors of ACE-inhibitor induced dry cough by Perindopril in 27,492 patients with vascular disease. Multivariate logistic regression analysis was used to study the incidence of cough in relation to baseline clinical characteristics including racial background. A simple clinical risk score composed of these 3 predictors of cough mounted to an odds ratio of 4.4 in the subjects with highest score (i.e. all determinants present). This large combined analysis of randomized clinical trials in 27,492 patients showed an overall lower incidence of cough leading to discontinuation of ACE-inhibitors (3.9%) as compared to literature. Clinical determinants of such cough are older age, female gender and concomitant use of lipid-lowering agents. In contrast, racial differences were not related to the incidence of cough.[37]

In the year 2014, Sidorenkov G and Navis G conducted a review on Safety of ACE inhibitor therapies in patients with chronic kidney disease. This paper reviews evidence from clinical studies regarding adverse effects of ACE inhibitors in patients with CKD. The safety aspects of ACE inhibitors are discussed in relation to their pharmacological action, drug-drug interactions, drug-diet interaction, and precautions needed in certain clinical conditions and other adverse effects. The main adverse effects of ACE inhibitors follow from their interaction with Renin-Angiotensin Aldosterone System (RAAS) activity and volume depletion. This interaction can be

turned into clinical benefit and increase efficacy of ACE inhibitors by reduction in dietary sodium or adding diuretics. The intensified treatment regimens based on ACE inhibitors can potentially improve renoprotection, but increase the risk of adverse effects. Better strategies to address safety concerns are needed. Introduction of clinical rules and safety indicators may help clinicians to identify hazardous co-prescriptions and adverse dietary habits and can decrease the frequency of adverse effects.[38]

In the year 2014, Pinargote P et al performed a study on ACE inhibitors induced upper respiratory symptoms. Study concluded that Cough and angioedema are well-known adverse reactions of ACE inhibitors. However, other adverse effects of upper airways such as postnasal drainage, rhinitis and nasal blockage, are less frequently recognised. These might share the same pathophysiological mechanism: bradykinin accumulation. We present two patients with ACE inhibitor-induced upper respiratory symptoms that improved after the discontinuation of ACE-inhibitors and substitution with angiotensin II receptor blockers. The incidence of these adverse events is not accurately known, since these are not required to be reported, but it is estimated to be low. This presents challenges to the physician and demonstrates the importance of keeping it as a differential diagnosis. Most physicians are aware of ACE inhibitor-induced cough but not of ACE inhibitor-induced nasal blockage, rhinitis or postnasal drainage. Identifying these can avoid unnecessary diagnostic tests and inappropriate treatment.[39]

In the year 2013,Nishida Y et al conducted a retrospective observational study on Comparative effect of angiotensin II type I receptor blockers on serum uric acid in hypertensive patients with type 2 diabetes mellitus. In Losartan users, mean SUA level was significantly decreased from baseline, while it was conversely increased in users of other ARBs; valsartan, telmisartan, candesartan and olmesartan. The mean reduction of SUA level from baseline was significantly greater in Losartan users compared with that in other ARB users. Comparison of ARBs other than Losartan showed no significant difference in mean change in SUA level from baseline. The study results shows that Losartan had the most beneficial effect on SUA level among five ARBs, and that there was no significant difference in the unfavourable effects on SUA level among four ARBs other than Losartan, at least during one year. These findings provide evidence of an effect of ARBs on SUA level, and support the benefit of the use of Losartan in hypertensive patients with type 2 DM. [40]

In the year 2013 , Heerspink HJ et al performed a post-hoc analysis on the effect of ramipril and telmisartan on serum potassium and its association with cardiovascular and renal events .A post-hoc analysis of the ONTARGET trial comparing dual therapy (ramipril and telmisartan) vsmonotherapy (ramipril or telmisartan) was performed. The main cardiovascular outcome was the composite of cardiovascular death, myocardial infarction, stroke, or hospitalization for heart failure. The renal outcome was defined as the composite of a doubling of serum creatinine or chronic dialysis. The association was independent of age, gender, diabetes, estimated glomerular filtration rate, systolic blood pressure and diuretic use. With the Precautions stipulated by the protocol of the ONTARGET trial, hypokalemia and

hyperkalemia were infrequent events. Nevertheless, both high and low serum potassium were associated with an increased risk of cardiovascular and renal disease.[41]

In the year 2012, Raebel MA conducted a review onHyperkalemia associated with use of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. Published incidence estimates of hyperkalemia associated with ACEi or ARB vary, but up to 10% of patients may experience at least mild hyperkalemia. Important Considerations when initiating ACEi or ARB therapy include obtaining an estimate of glomerular filtration rate and a baseline serum potassium concentration, as well as assessing whether the patient has excessive potassium intake from diet, supplements, or drugs that can also increase serum potassium. Serum potassium monitoring shortly after initiation of therapy can assist in preventing hyperkalemia. If hyperkalemia does develop, prompt recognition of cardiac dysrhythmias and effective treatment to antagonize the cardiac effects of potassium, redistribute potassium into cells, and remove excess potassium from the body is important. Understanding the mechanism of action of ACEi and ARB coupled with judicious drug use and clinical vigilance can minimize the risk to the patient of developing hyperkalemia.[42]

In the year 2012, Cosentino M et al conducted a study onincreased reporting of adverse reactions to ACE inhibitors associated with limitations to drug reimbursement for angiotensin-II receptor antagonists. 228 reports of ACE inhibitor-associated ADRs, and cough was the ADR reported in 93.4% of cases. There were no reports of cough in 2007, 50 in 2008, 156 in 2009 and 7 in 2010. In 2008-2009, the dispensation of ACE inhibitors showed little variation, while that of AT1 receptor

antagonists grew about twofold. There was a clear correlation between ACE inhibitor-associated ADR reporting and limitation to AT1 receptor antagonist reimbursement status. Drug reimbursement policies should thus be added to the list of factors that may bias ADR reporting, and health authorities should be aware of this potential bias when defining specific measures to regulate prescription and use of new drugs.[43]

In the year 2012, Uday Venkat Mateti et alperformed a study on Pattern of Angiotensin-Converting Enzyme Inhibitors Induced Adverse Drug Reactions in South Indian Teaching Hospital. Their study was conducted to evaluate the incidence of ADRs due to angiotensin-converting enzyme Inhibitors in cardiology department. A cross-sectional observational study was carried out for a period of 6 months. Causality assessment showed that majority of ADRs was probable and were found to be moderately severe. The study concludes geriatrics and female patients have higher incidence of ADRs. So early identification and management of ADRs are essential for this population.[44]

In the year 2012, Norman M Kaplanperformed a literature survey on Major side effects of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers. Side effects that occur with ACE inhibitors are related to either reduced angiotensin II formation or increased kinins. Those related to reduce angiotensin II formation include hypotension, acute renal failure, hyperkalemia and problems during pregnancy. Side effects thought to be related, at least in part, to increased kinins include cough, angioedema, and anaphylactic reactions. Hyperkalemia and renal failure may require termination of the ACE inhibitor. Treatment consists of

lowering the dose or discontinuing the drug. Readministration of the drug is associated with a high rate of recurrent cough .Angioedema is rare but potentially fatal complication of ACE inhibitors. Angioedema may also occur with ARBs but the risk is lower .Patients who are on both an ACE inhibitor and an ARB are at higher risk for adverse effects. Thus, combined therapy should not be considered in the treatment of hypertension or other disorders unless there is compelling evidence of benefit.[45]

In the year 2010,Nishant V. Sangole and Vaishali N. Dadkar conducted a study on ADR monitoring with ACE inhibitor. One hundred and twenty patients with essential hypertension were randomized into four groups receiving Enalapril, Lisinopril, Ramipril, and Fosinopril. They were followed up for four months, to observe the clinical efficacy along with the associated ADRs.Mild, dry brassy cough (% incidence; 95% CI) was observed with d-ACEIs (6.6%; 0 to 15.6) versus p-ACEI (20%; 5.7 to 34.3), in which the cough observed was moderate-to-severe in intensity and two patients required treatment discontinuation (P <0.05).The authors concluded that the Phosphonate group in p-ACEIs may have a probable relationship with increase in the incidence and severity of ADRs such as dry brassy cough and hypotension. The di-carboxyl group in d-ACEIs may have a probable relationship with increase in the incidence of ADRs like nausea.[46]

In the year 2008, Shibata MC et al Conducted a systemic review on the effects of angiotensin-receptor blockers on mortality and morbidity in heart failure. Mortality data were available from 27,495 patients. The Author concluded that Angiotensin II receptor blockers did not show any beneficial effect on mortality when

used in combination with ACE-I or when compared with ACE-I alone. A 17% reduction in hospital admissions was observed.[47]

In the year 2008, Matchar DB et al conducted a systemic review on comparative effectiveness of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers for treating essential hypertension. 61 clinical studies that directly compared ACE inhibitors versus ARBs in adult patients with essential hypertension were included. A standardized protocol with predefined criteria was used to extract data on study design, interventions, population characteristics, and outcomes; evaluate study quality and applicability; and assess the strength of the body of evidence for key outcomes.ACE inhibitors and ARBs had similar long-term effects on blood pressure (50 studies; strength of evidence, high). Consistent fair- to good-quality evidence showed that ACE inhibitors were associated with a greater risk for cough. There were fewer withdrawals due to adverse events and greater persistence with therapy for ARBs than for ACE inhibitors, although this evidence was not definitive. Available evidence shows that ACE inhibitors and ARBs have similar effects on blood pressure control, and that ACE inhibitors have higher rates of cough than ARBs. Data regarding other outcomes are limited.[48]

In the year 2006, Overlack A performed a study on Incidence, mechanisms and management of ACE inhibitor-induced cough and bronchospasm. Cough has emerged as a class effect occurring with all ACE inhibitors with no clear difference between the single substances. While ACE inhibition is safe in the vast majority of

patients with obstructive airways disease, asthmatic symptoms or exacerbation of asthma as well as a rise in bronchial reactivity have been occasionally reported. ACE inhibition increases the cough reflex. The mechanisms underlying ACE

inhibitorinduced cough are probably linked to suppression of kininase II activity, which may

befollowed by an accumulation of kinins, substance P and prostaglandins. Physicians should be aware that a dry cough is the most common adverse effect of ACE inhibitors and that this symptom may occur not necessarily shortly afterinstitution of therapy but months or even a year later. Replacement by another ACE inhibitor should not be tried, since the cough will almost always recur on rechallenge with the same or another ACE inhibitor. After withdrawal of the ACE inhibitor, which is the treatment of choice, cough will resolve usually within a few days.[49]

In the year 2004, Fogari Rand Zoppi A conducted a study on effect of antihypertensive agents on quality of life in the elderly. Calcium channel antagonists have generally been associated with a positive effect on quality of life, although some trials have shown high rates of adverse effects and withdrawals, particularly with first-generation dihydropyridines. They have been demonstrated not to interfere with or even improve cognitive function as well as sexual performance. Although no class of antihypertensive agents presents a clearly superior effect over the others in terms of quality of life, the current impression is that ACE inhibitors and angiotensin II receptor antagonists may offer some advantage, at least in regard to effects on cognitive function and sexual activity.[50]

In the year 2002,Ahmed Aconducted a study to determine the association between the early rises in serum creatinine levels associated with the use of Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) and the long-term renoprotective properties of these drugs in patients with

chronic renal insufficiency. Patients with normal renal function were likely to show a much smaller rise in serum creatinine level (approximately 10% above the baseline of 0.9 mg/dL), mostly occurring during the first week after initiation of therapy, with subsequent stabilization, whereas patients with normal renal function suffering from heart failure, volume depletion, or bilateral renal artery stenosis experienced a significant rise (approximately 225% above baseline) in serum creatinine level. Patients with chronic renal insufficiency (serum creatinine>1.5 mg/dL) who received therapy with ACE inhibitors had about a five times higher risk of developing hyperkalemia than those with normal renal function, whereas presence of heart failure increased the risk of hyperkalemia by about three times over those without heart failure. The authors recommend that ACE inhibitor therapy should not be discontinued unless serum creatinine level rise above 30% over baseline during the first 2 months after initiation of therapy or hyperkalemia (serum potassium level >or=5.6 mmol/L) develops. [51]

In the year 2001, Alice Schmidt et al conducted a prospective study on the effect of ACE inhibitor and angiotensin II receptor antagonist therapy on serum uric acid levels and potassium homeostasis in hypertensive renal transplant recipients treated with CsA. In this prospective, open, randomized, two-way cross-over study we included 13 hypertensive CsA-treated patients after renal transplantation and administered either the angiotensin-converting enzyme (ACE) inhibitors enalapril or Losartan. Serum aldosterone and urinary aldosterone excretion were significantly reduced only during ACE inhibitor treatment, which might explain the variable effects on potassium homeostasis. Losartan may be a useful agent to reduce blood pressure and serum uric acid levels in renal transplant recipients treated with CsA.

Furthermore, in this high-risk population, the effects on serum potassium levels are less marked with Losartan than with enalapril.[52]

In the year 1996, Kubota k. et al conducted a prescription event monitoring on cough induced by ACE inhibitor. Several factors which had obscured the causal relationship in the individual cases were found to be also an obstacle in PEM. For example, cough was a common and non-serious event and was under-reported in the PEM study of enalapril and the rate was not strikingly different from that recorded for other drugs. Cough induced by ACE-inhibitors has several characteristics which reduce the chance of a recognisable 'signal'. The original questionnaires returned from doctors in the PEM study of enalapril have been re-examined. The observation that the rate of cough diminished after enalapril had been stopped rather than increased after starting, provided the best evidence of causality, because this was not affected by many biases such as the publicity that had occurred prior to doctors participating in PEM completed later reports.[53]

In the year 1990, Moser M conducted a prospective study on relative effectiveness and adverse reactions of Antihypertensive medications. It was found Thiazide diuretics may be more effective as antihypertensive agents in many subsets of patients than other medications, especially in reducing systolic blood pressure. Angiotensin converting enzyme (ACE) inhibitors and beta-blockers are less effective than calcium blockers or diuretics in black, beta-blockers may be less effective in the elderly. When used as initial monotherapy, most available antihypertensive drugs produce significant adverse subjective effects in about 8-10% of patients; centrally acting drugs, however, may produce annoying side effects in 20-30% of patients.

Diuretics are recommended as the second drug of choice if one of the other agents is used first. With this approach approximately 80% or more of patients can be controlled at normotensive levels on one or at most two drugs.[54]

3. AIM AND OBJECTIVES

3.1. Aim

The aim of the study wasto investigate the incidence and prevalence of drug related outcomes in hypertensive patients on ACE inhibitors.

3.2. Objectives

The objectives of the study were

- To assessthe incidences of cardiac events in patients with ACE inhibitor therapy
- To assess the prevalence of liver diseases and hyperuricaemia in hypertensive patients with ACE inhibitors.

4. NEED FOR THE STUDY

ACE inhibitors are the first choice of drugs in all grades of essential as well as renovascular hypertension. Although many research have been done so far to assess the antihypertensive efficacy of ACE inhibitors they have serious adverse effects related to it like angioedema, hypotension, hyperkalaemia, sleep disturbances, hyperuricaemia, cough, rashes, urticaria etc.

Many epidemiological studies and supportive literature states that these ACE Inhibitors induced adverse events are one of the important reasons for persistent morbidity and mortality in developed countries. But in developing countries like India the reported cases of incidence of drug related side effects due to ACE inhibitors are less compared that of developed countries. But studies shows that, since much hypertensive patients are in India the actual incidence of specific adverse events in hypertension goes unreported and the actual epidemiology in India is not well understood.

We designed this study in an attempt to understand the incidence of cardiac events and prevalence of hyperuricaemia and liver diseases in hypertensive patients on ACE inhibitorswhich were expected to be reported among rural population ata multispecialty hospital in Namakkal district.

5. SCOPE OF THE STUDY

The study was conducted enrolling all the male and female patients strictly on the basis of underlying disease (i.e.) hypertension, age and medication prescribed with ACE inhibitors. So we expect the results to be unbiased and confounding.

The study was expected to give clear report on the incidence of cardiac events, and prevalence of hyperuricaemia and liver disease since it was conducted in hospital located in rural region as we expect the results to be more reliable, repeatable and reproducible.

6. PLAN OF WORK

The proposed study entitled “An investigation on the incidenceand prevalence of drug related outcomes in hypertensive patients under ACE inhibitor therapy”was planned and carried out in a tertiary care hospital as given below.

Phase I

- Identification of research problem and scope of the study
- Literature survey
- Preparation of study protocol
- Obtaining ethical clearance from the hospital authorities

Phase II

- Design of structured pro-forma
- Patient selection
- Obtaining patient consent
- Data retrieval from the cardiology and general medicine department.

Phase III

- Data analysis
- Report submission

7. METHODOLOGY

7.1 STUDY DESIGN

Prospective observational study

7.2 STUDY CENTRE

Department of General medicine and cardiology inVivekananda Medical Care Hospital, Tiruchengodu.

7.3 STUDY DURATION

July 2016 – June 2017 (12months)

7.4 ETHICAL COMMITTEE APPROVAL

The study protocol was approved by the institutional ethics committee of Vivekanandha Medical Care Hospital (Ref.No:SVCP/IEC/JAN/2016/13) (Annexure – 1)

7.5 SAMPLE POPULATION

Total 230 patients who are having hypertension and under ACE inhibitor therapy were screened and 112 records were selected based on the following inclusion and exclusion criteria for further study.

7.6 INCLUSION CRITERIA

- Patients of both the genders of more than 18years in age
- Patients with Hypertension prescribed with ACE inhibitors
- Both in and out patients

7.7 EXCLUSION CRITERIA

- Patients who are not willing to participate in the study
- Pregnant and Lactating females
- Patients with insufficient data in their records

7.8 DATA COLLECTION

Consent was obtained from each subject in Patient Consent form before initiating the study. Structured pro-forma was used to collect various clinical and demographic details of the patients such as age, gender, reason for admission, past medical history, past medication history, vital signs, lab investigations, primary diagnosis and treatment chart. Treatment data including prescribed drugs, doses, frequency and route of administration were also recorded.

7.9 METHOD

Patients were assessed at baseline with respect to age, gender, BMI, co-morbidity conditions, ACE inhibitors prescribed and duration of therapy. Patient was followed up for 6 months. The incidences of cardiac events wereidentified and prevalence of hyperuricaemia and liver diseases wereanalysed.

7.11 STATISTICS

The statistical analysis was done using Microsoft excel. All the datas were expressed in percentage. Collected data's were entered in Microsoft excel spreadsheet for further interpretations.

8. RESULTS

A total of 230 patients who are having hypertension and taking ACE inhibitors in cardiology and general medicine department were screened and 112 records were selected based on the inclusion and exclusion criteria.

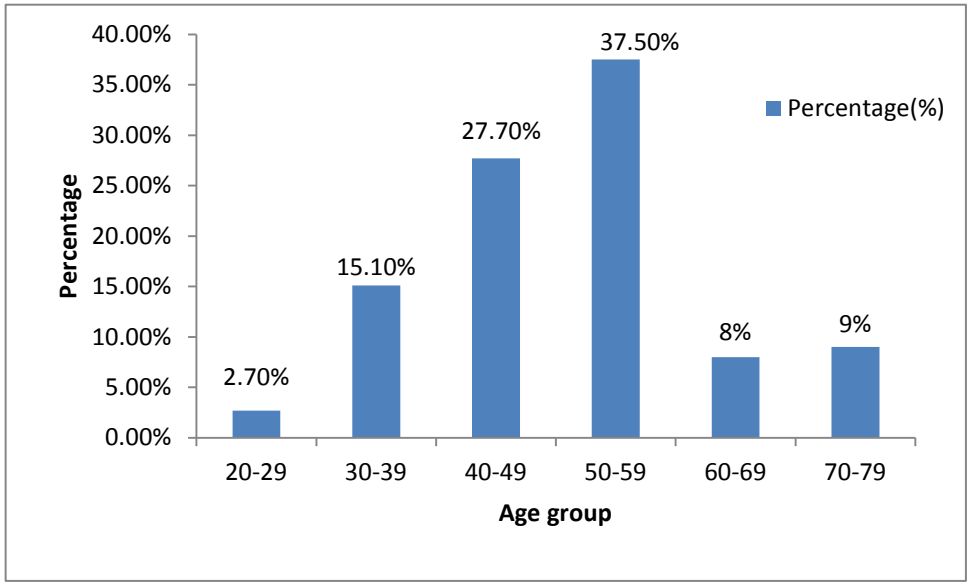
8.1. AGE WISE DISTRIBUTION OF THE STUDY POPULATION

Out of 112 cases, 2.7% (3) were in the age group of 20-29 years, 15.1.% (17) were in the age group of 30-39 years, 27.7% (31) were in the age group of 40-49 years, 37.5% (42) were in the age group of 50-59 years, 8% (9) were in the age group of 60-69 years and 9% (10) were in the age group of 70-79 years. Mean age of the study population was 55.7 ± 6years. (Table 1, Figure 1)

Table 1. Age wise distribution of the study population (n=112)

S.No.	Age (years)	No of Patients	Percentage(%)
1.	20-29	3	2.7 %
2.	30-39	17	15.1%
3.	40-49	31	27.7%
4.	50-59	42	37.5%
5.	60-69	9	8%
6.	70-79	10	9%

Figure 1. Age Wise distribution of the study population (n=112)



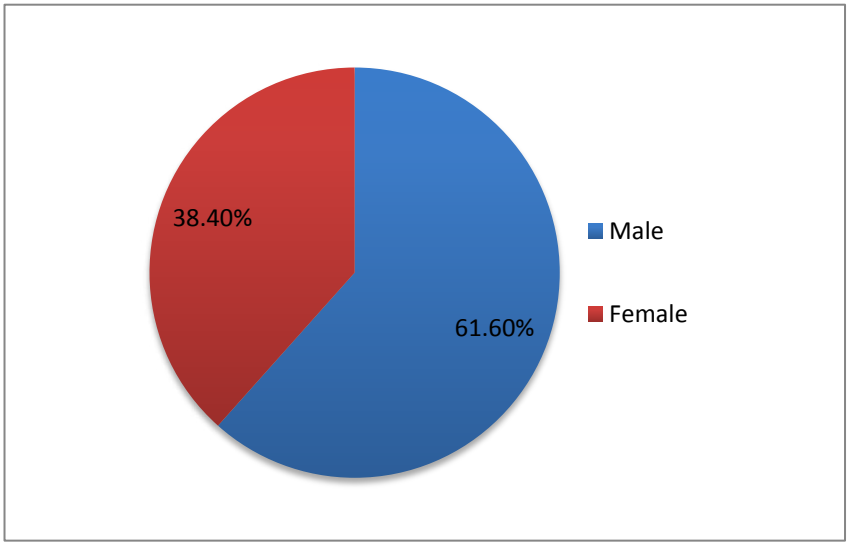
8.2 GENDER WISE DISTRIBUTION AMONG THE STUDY POPULATION

A total of 112 hypertensive patients, males were 61.6% (69) and females were 38.39% (43). (Table 2, Figure 2)

Table 2. Gender wise distribution of the study population (n=112)

Gender	Number of Patients	Percentage
Male	69	61.6 %
Female	43	38.4 %

Figure 2. Gender wise distribution among the study population (n=112)



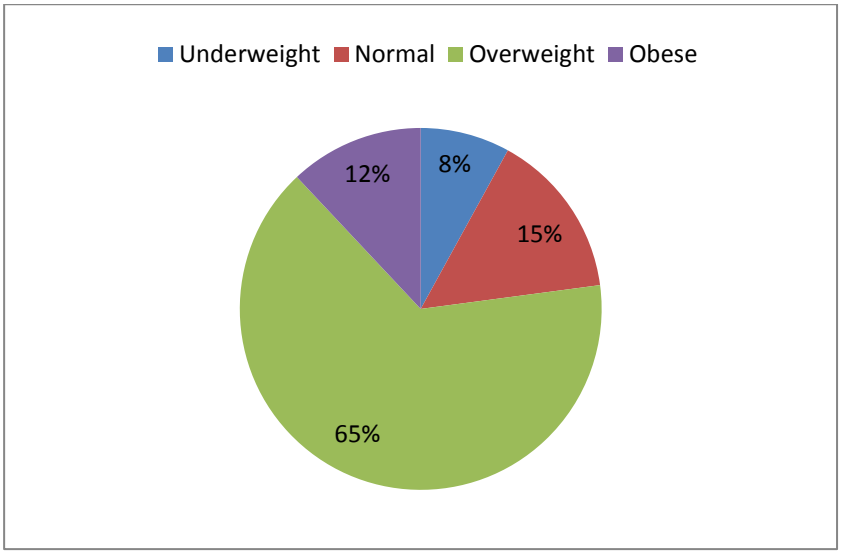
8.3. BODY MASS INDEX OF THE STUDY POPULATION

A total of 112 patients, 8% (9 were in normal body weight, 14.9% (16) were Under Weight, 65.1% (74) were overweight and 12% (13) were Obese. (Table 3, Figure 3)

Table 3. BMI among the study population (n=112)

BMI	Number of Patients	Percentage
Underweight	9	8%
Normal	16	14.9%
Overweight	74	65.1%
Obese	13	12%

Figure 3. BMI among the study population (n=112)



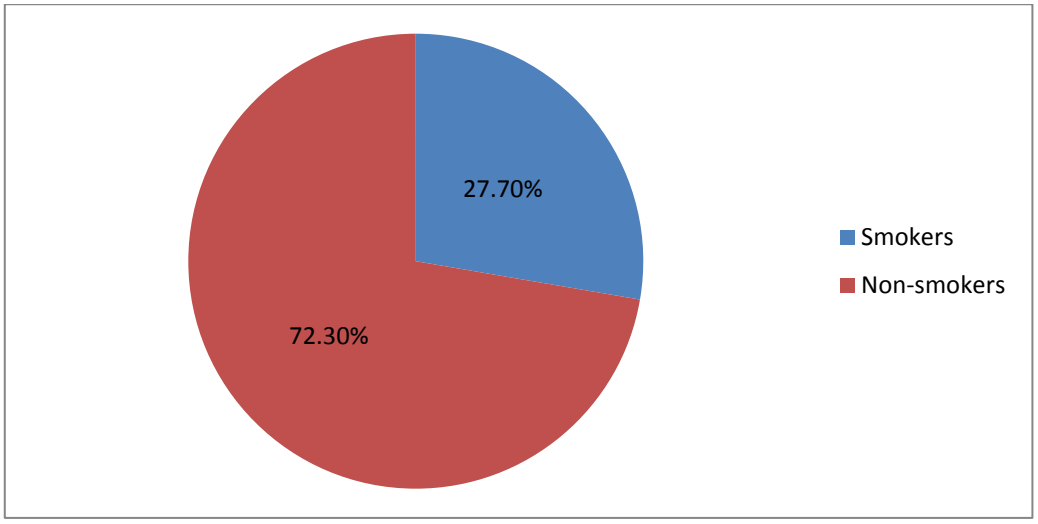
8.4. SOCIAL HABITS OF THE STUDY POPULATION

Out of 112 patients, 27.7% (31) were smokers and 72.3% (81) were non smokers. (Table 4, Figure 4)

Table 4. History of smoking among the study population (n=112)

Smoking habits	Number of Patients	Percentage
Smokers	31	27.7%
Non-smokers	81	72.3%

Figure 4. History of smoking among the study population (n=112)

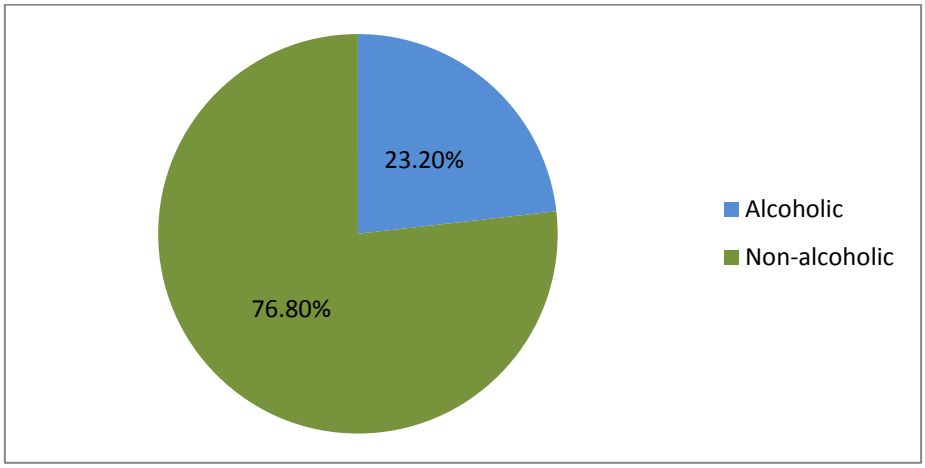


Out of 112 patients, 23.2% (26) were alcoholic and 76.8% (86) were non alcoholic, (Table 5, Figure 5)

Table 5. History of alcoholism among the study population (n=112)

Alcoholic habits	Number of Patients	Percentage
Alcoholic	26	23.2%
Non-alcoholic	86	76.8%

Figure 5. History of alcoholism among the study population (n=112)



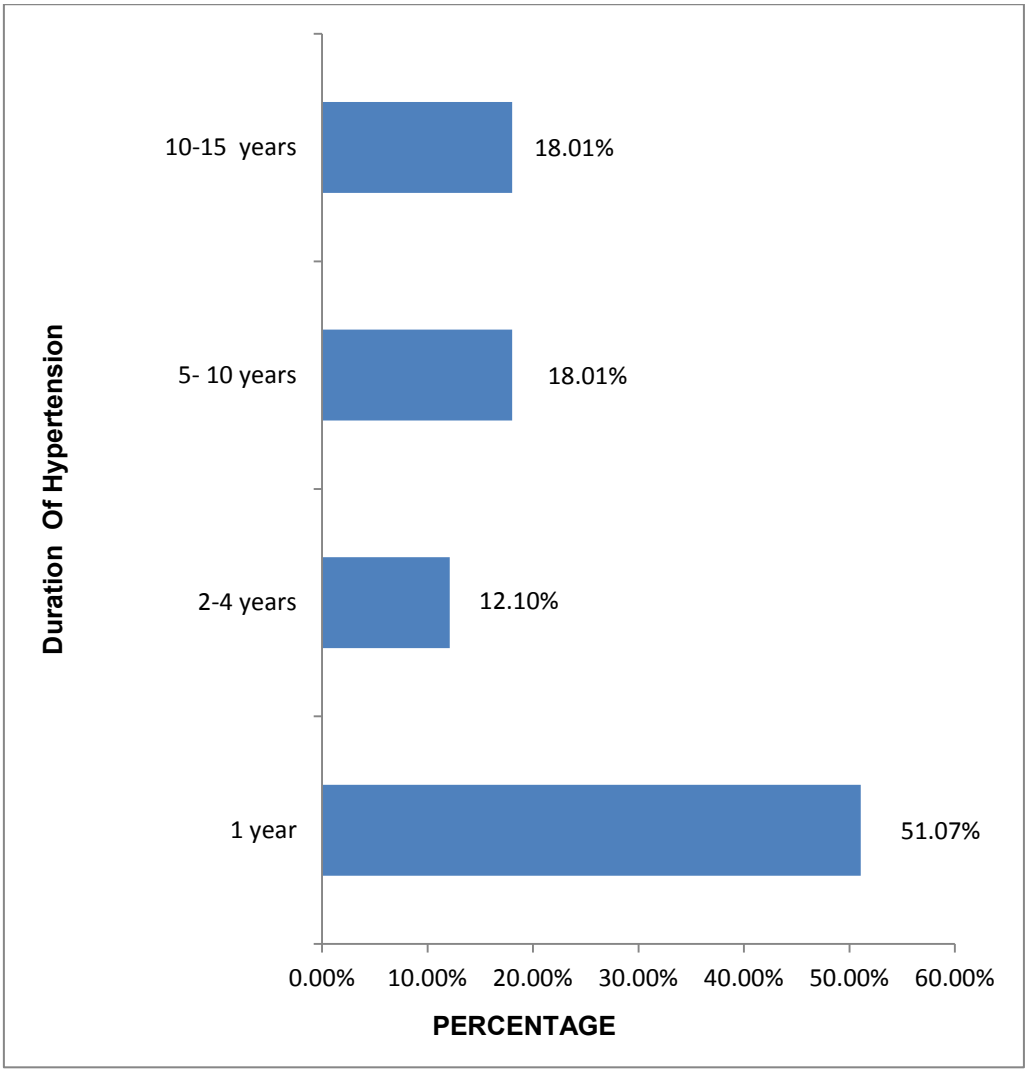
8.6. DURATION OF HYPERTENSION AMONG THE STUDY POPULATION

A total of 112 patients, 51.07% (59) were having 1 year duration of Hypertension, 12.1% (13) were having 2-4 years duration of Hypertension, 18.01% (20) were having 5-10 years duration of hypertension, 18.01% (20) were having 10-15 years duration of Hypertension (Table 6,figure 6)

Table 6. Duration of hypertension among the study population (n=112)

Duration of Hypertension	Number of Patients	Percentage
1 year	59	51.07%
2-4 years	13	12.1%
5- 10 years	20	18.01%
10-15 years	20	18.01%

Figure 6. Duration of hypertension among the study population (n=112)



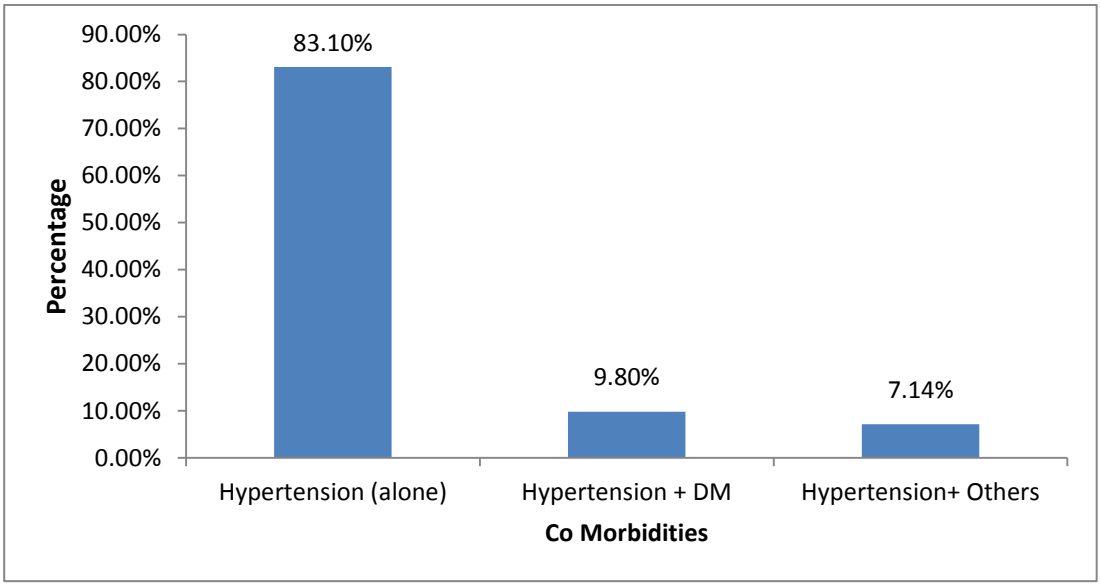
8.7. PATTERN OF PREVALENCE OF CO-MORBIDITIES AMONG THE STUDY POPULATION

A total of 112 patients, 83.1% (93) were having hypertension alone, 9.8% (11) were hypertension with diabetes mellitus, and 7.14% (8) have hypertension with other complications. (Table 7, figure 7)

Table 7. Pattern of co-morbidities prevalence among the study population (n=112)

Co-Morbidities	Number of Patients	Percentage
Hypertension (alone)	93	83.1%
Hypertension + DM	11	9.8%
Hypertension+ Others	8	7.14%

Figure 7. Pattern of co-morbidities prevalence among the study population (n=112)



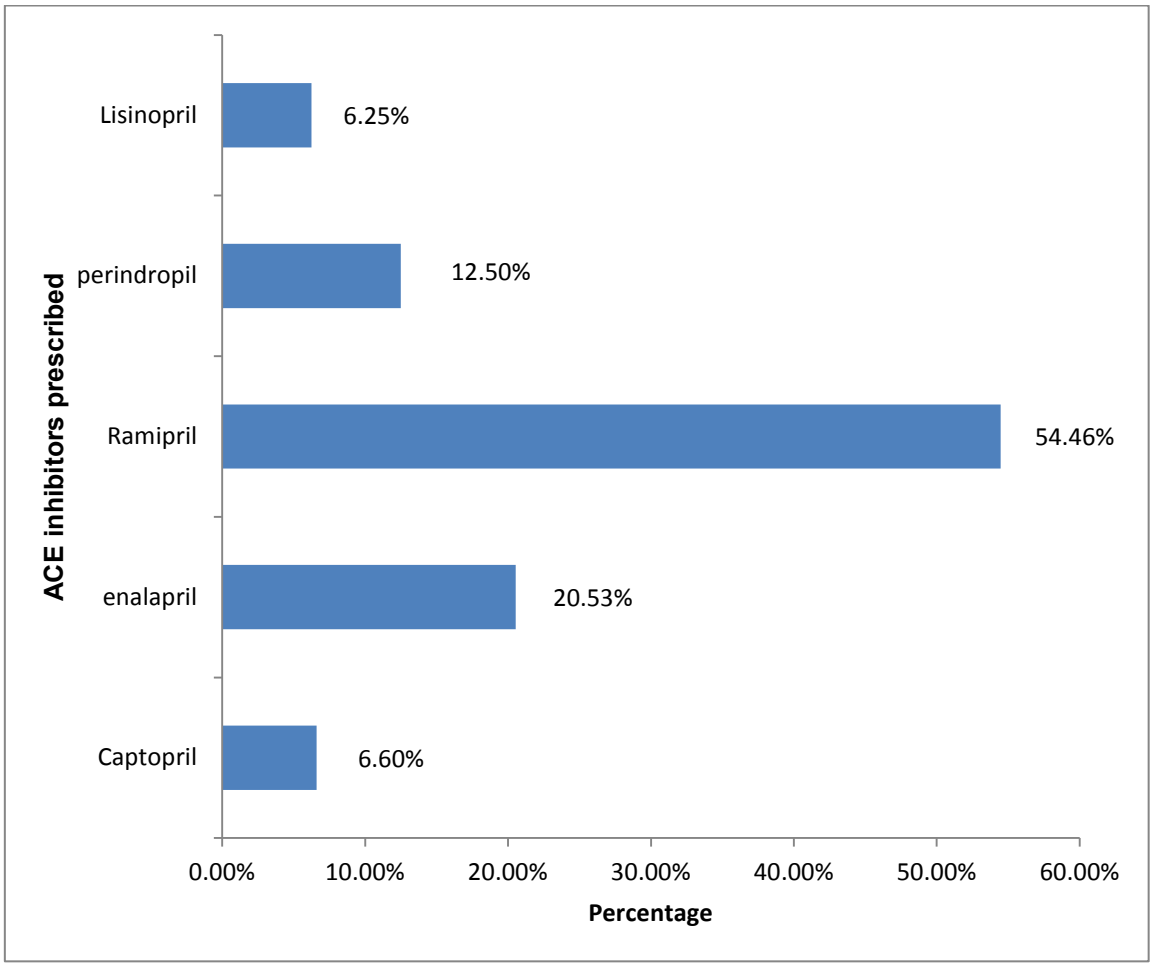
8.8. ACE INHIBITORS PRESCRIBED IN THE STUDY POPULATION

A total of 112 patients, 6.6% (7) prescribed with captopril, 20.53% (23 patients) prescribed with enalapril, 54.46 %(61) prescribed with Ramipril, 12.5% prescribed with (14) prescribed with Perindopril and 6.25% (7) prescribed with Lisinopril. (Table 8, Figure 8)

Table 8. Ace inhibitors prescribed in the study population (n=112)

S. No	ACE Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage
1.	Captopril	50mg	TD	7	6.6%
2.	Enalapril	10mg	OD	23	20.53%
3.	Ramipril	1.25mg 2.5 mg	OD	61	54.46%
4.	Perindopril	20mg	OD	14	12.5%
5.	Lisinopril	40mg	OD	7	6.25%

Figure 8. ACE inhibitors prescribed in the study population (n=112)



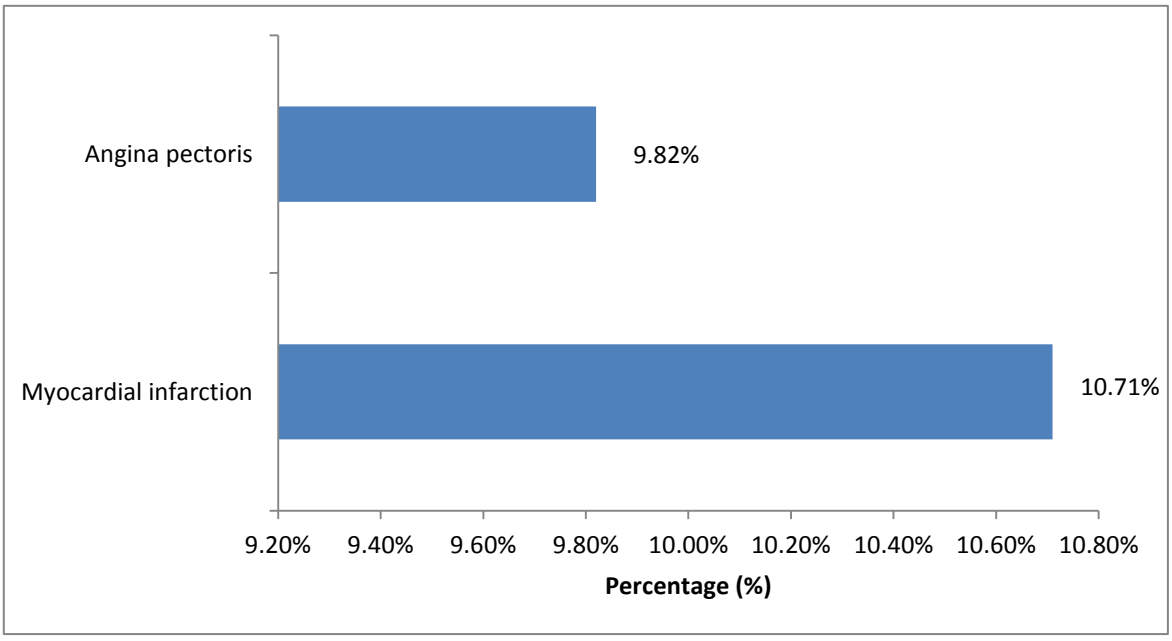
8.9. ASSESSMENT OF INCIDENCE OF CARDIAC EVENTS IN THE STUDY POPULATION

Out of 112 patients incidence of cardiac events found in Hypertensive patients who are under ACE inhibitors were 23, in which 10.71% (12) had myocardial infarction and 9.82% (11) had Angina pectoris. (Table 9, Figure 9)

Table 9. Incidence of cardiac events in the study population (n=112)

Cardiac events	No. of patients	Percentage (%)
Myocardial infarction	12	10.71%
Angina pectoris	11	9.82%
Total	23	100 %

Figure 9. Incidence of cardiac events in the study population (n=112)



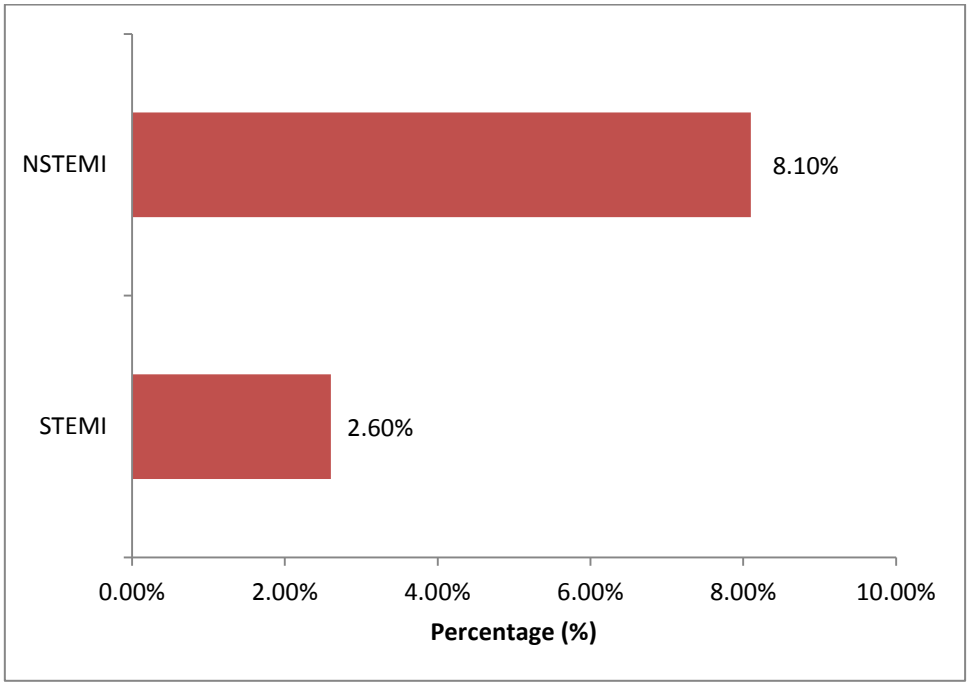
8.10. INCIDENCE OF MYOCARDIAL INFARCTION

Among 12 patients with incidence of myocardial infarction 2.6% (3) were having STEMI and 8.1 % (9) were having NSTEMI. (Table 10, Figure 10)

Table 10. Incidence of myocardial infarction based on type (n=112)

Myocardial infarction	No. of patients	Percentage (%)
STEMI	3	2.6%
NSTEMI	9	8.1%

Figure 10. Incidence of myocardial infarction based on type (n=112)



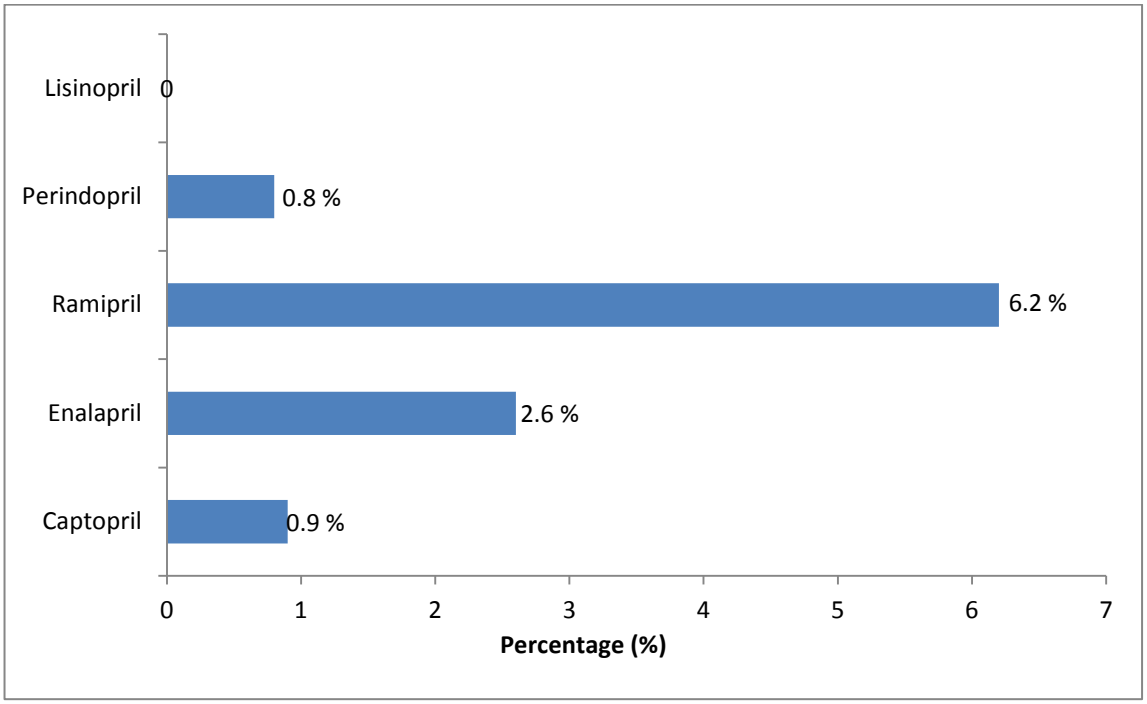
8.11. INCIDENCE OF MYOCARDIAL INFARCTION IN PATIENTS ON ACE INHIBITORS

Out of 12 patients with incidence of MI with ACE inhibitors 0.9% (1) prescribed with Captopril, 2.6% (3) with Enalapril, 6.3% (7) with Ramipril, 0.8% (1) with Perindopril. (Table 11, Figure 11)

Table 11. Incidence of Myocardial Infarction in Patients on ACE Inhibitors (n=112)

S. no.	ACE Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage
1	Captopril	50mg	TD	1	0.9 %
2	Enalapril	10mg	OD	3	2.6%
3	Ramipril	1.25mg	OD	3	2.6%
		2.5 mg		4	3.6%
4	Perindopril	20mg	OD	1	0.8%
5	Lisinopril	40mg	OD	0	0%

Figure 11. Incidence of Myocardial Infarction in patients on ACE inhibitors (n=112)



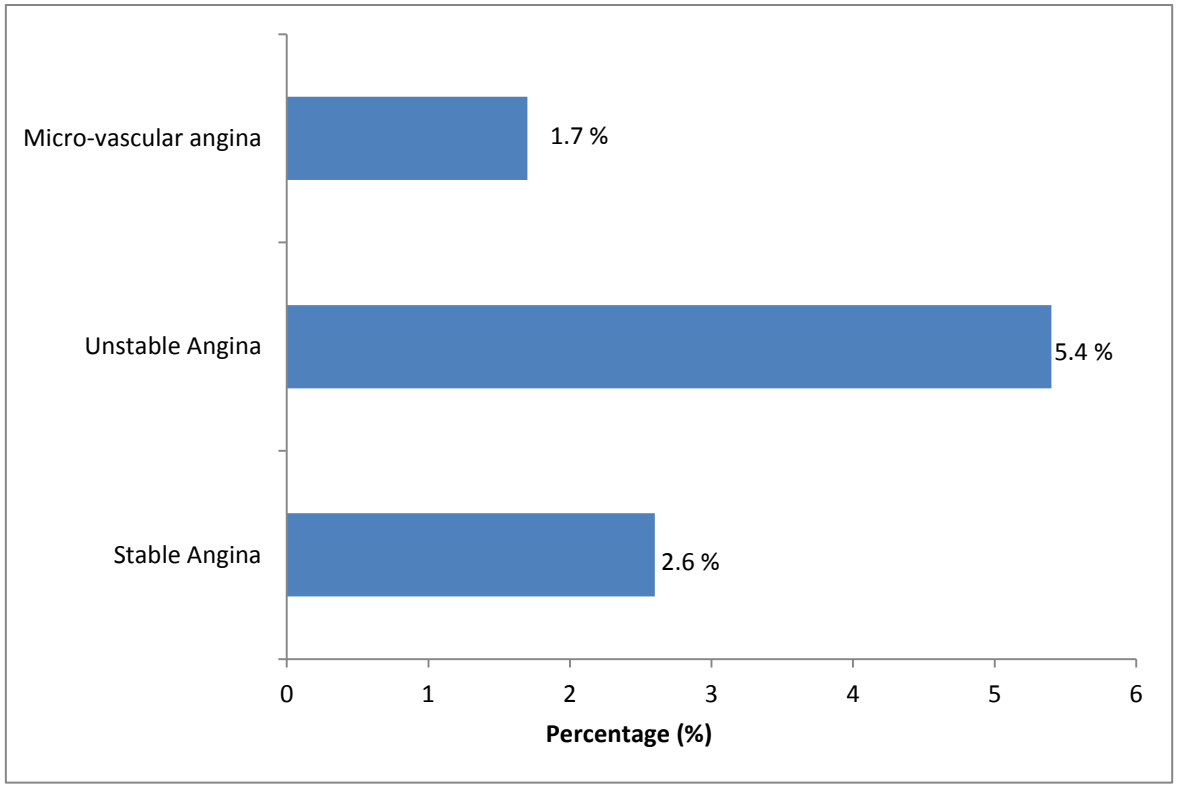
8.12. INCIDENCE OF ANGINA PECTORIS BASED ON TYPE

Among 112 patients in the study population 11 patients were having Angina pectoris in which 2.6% (3) are having stable angina, 5.4% (6) were having unstable Angina, 1.7% (2) having micro vascular angina. (Table12, Figure12)

Table 12. Incidence of Angina Pectoris based on Type

Cardiac events	No. of patients	Percentage (%)
Stable Angina	3	2.6 %
Unstable Angina	6	5.4%
Micro-vascular angina	2	1.7%

Figure 12. Incidence of Angina pectoris based on Type



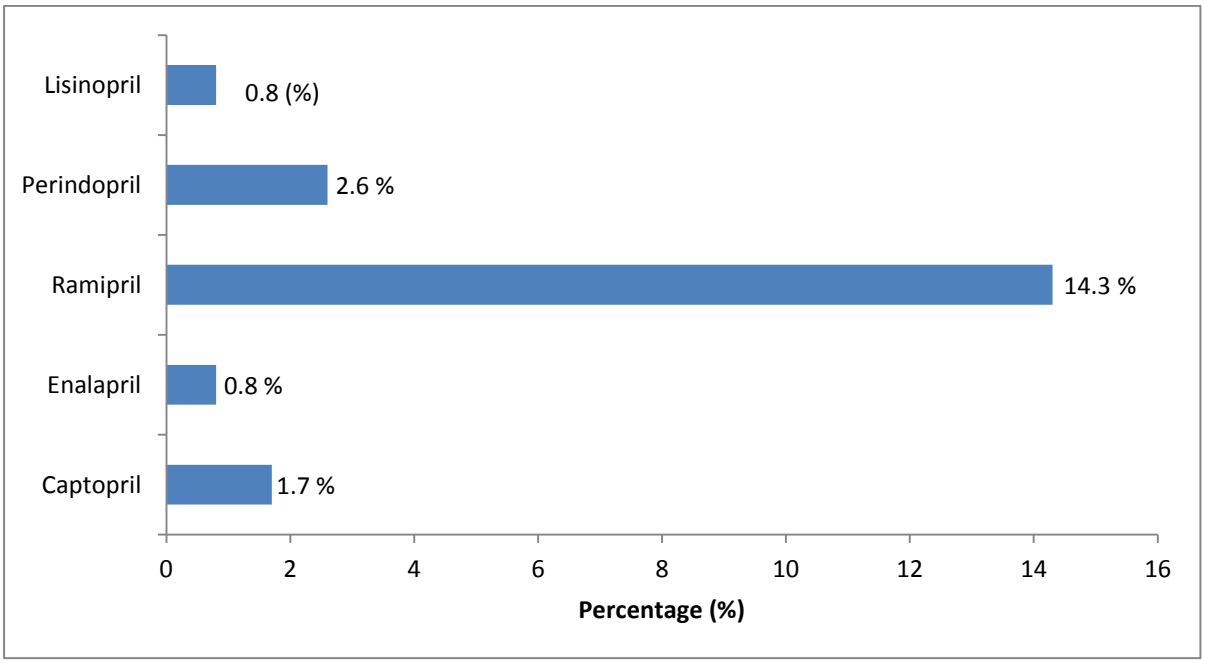
8.13. INCIDENCE OF ANGINA PECTORIS IN PATIENTS ON ACE INHIBITORS

Among 11 patients, Incidence of Angina pectoris on ACE inhibitors 1.7% (2patients) prescribed with Captopril, 0.8% (1) with Enalapril, 4.4% (5) with Ramipril, 2.6% (3) with Perindopril and 0.8% (1) with Lisinopril. (Table 13, Figure 13)

Table 13. Incidence of Angina Pectoris in patients on ACE inhibitors (n=112)

S. No.	ACE Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage (%)
1.	Captopril	50mg	TD	2	1.7 %
2.	Enalapril	10mg	OD	1	0.8%
3.	Ramipril	1.25mg	OD	3	2.6%
		2.5 mg		2	1.7%
4.	Perindopril	20mg	OD	3	2.6%
5.	Lisinopril	40mg	OD	1	0.8%

Figure 13. Incidence of Angina pectoris in patients on ACE inhibitors (n=112)



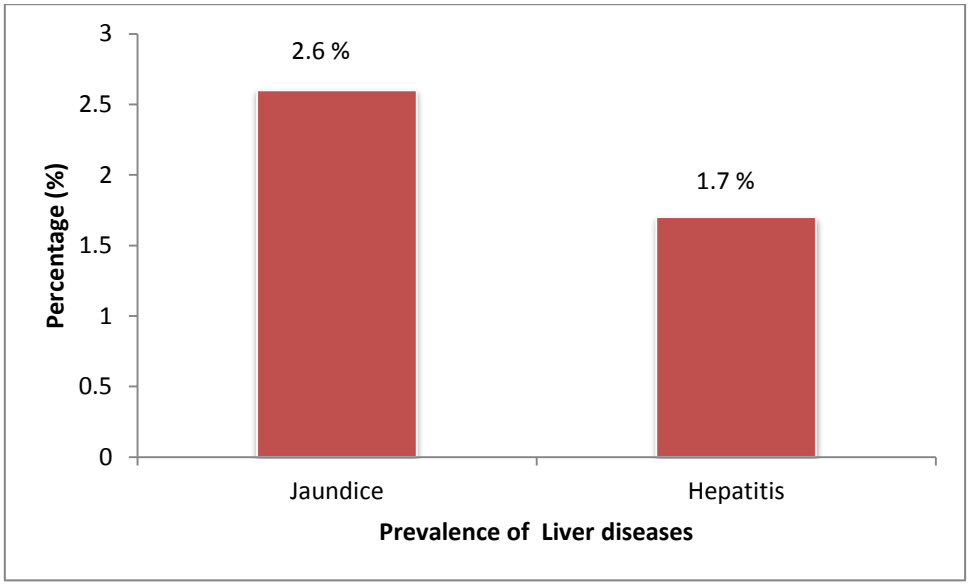
8.14. ASSESSMENT OF PREVALENCE OF LIVER DISEASES

Out of 112 patients prevalence of liver diseases on ACE inhibitors were found in 5 in which 2.6% (3) are having jaundice and 1.7% (2) are having hepatitis (Table 14, Figure 14)

Table 14. Prevalence of liver diseases

Liver diseases	No. of patients with prevalence	Percentage (%)
Jaundice	3	2.6 %
Hepatitis	2	1.7%

Figure 14. Prevalence of Liver diseases



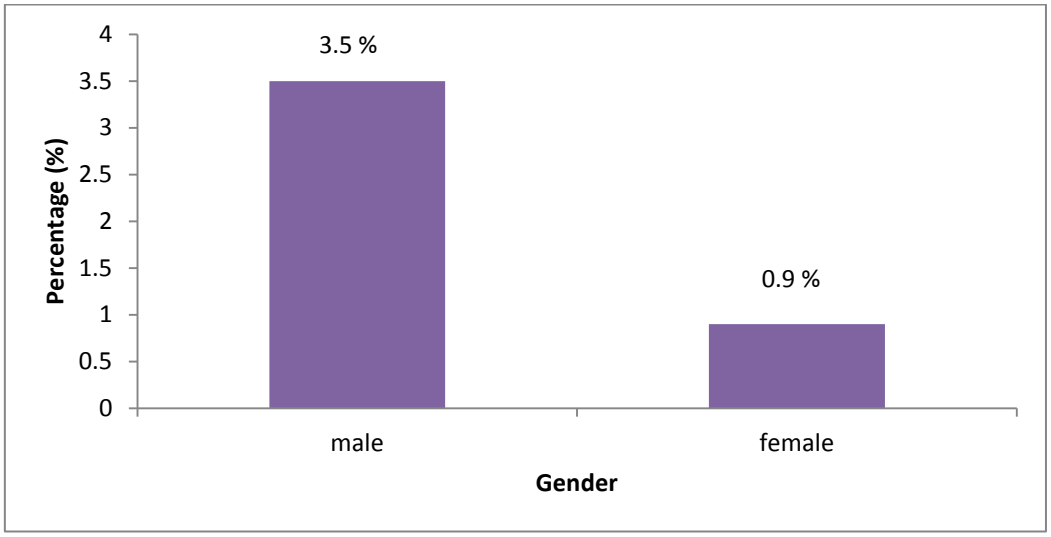
8.15. PREVALENCE OF LIVER DISEASES BASED ON GENDER

Among 5 patients having prevalence of liver diseases, 3.5% (4) are male and 0.9% (1) was female. (Table 15, Figure 15)

Table 15. Prevalence of Liver diseases based on Gender (n=112)

Gender	No. of patients with prevalence	Percentage (%)
male	4	3.5 %
female	1	0.9%

Figure 15 -Prevalence of Liver diseases based on Gender (n=112)



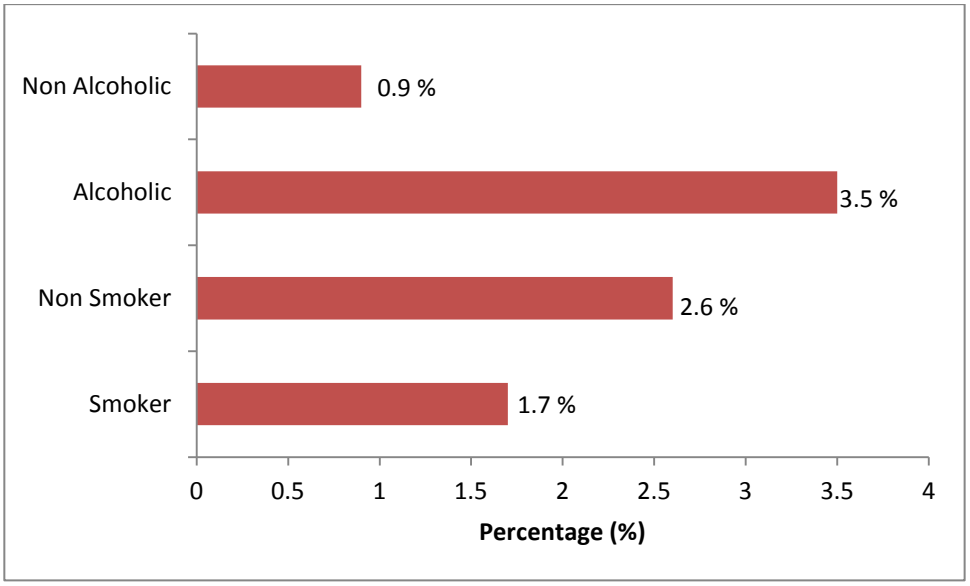
8.16. PREVALENCE OF LIVER DISEASES BASED ON SOCIAL HISTORY

Among 5 patients having prevalence of liver diseases 1.7% (2) were smokers and 2.6% (3) were non smokers, 3.5% (4) were alcoholic and 0.9% (1) was non alcoholic. (Table 16, Figure 16)

Table 16. Prevalence of liver diseases based on social history (n=112)

Social history	No. of patients with prevalence	Percentage (%)
Smoker	2	1.7%
Non Smoker	3	2.6%
Alcoholic	4	3.5%
Non Alcoholic	1	0.9%

Figure 16. Prevalence of liver diseases based on social history (n=112)



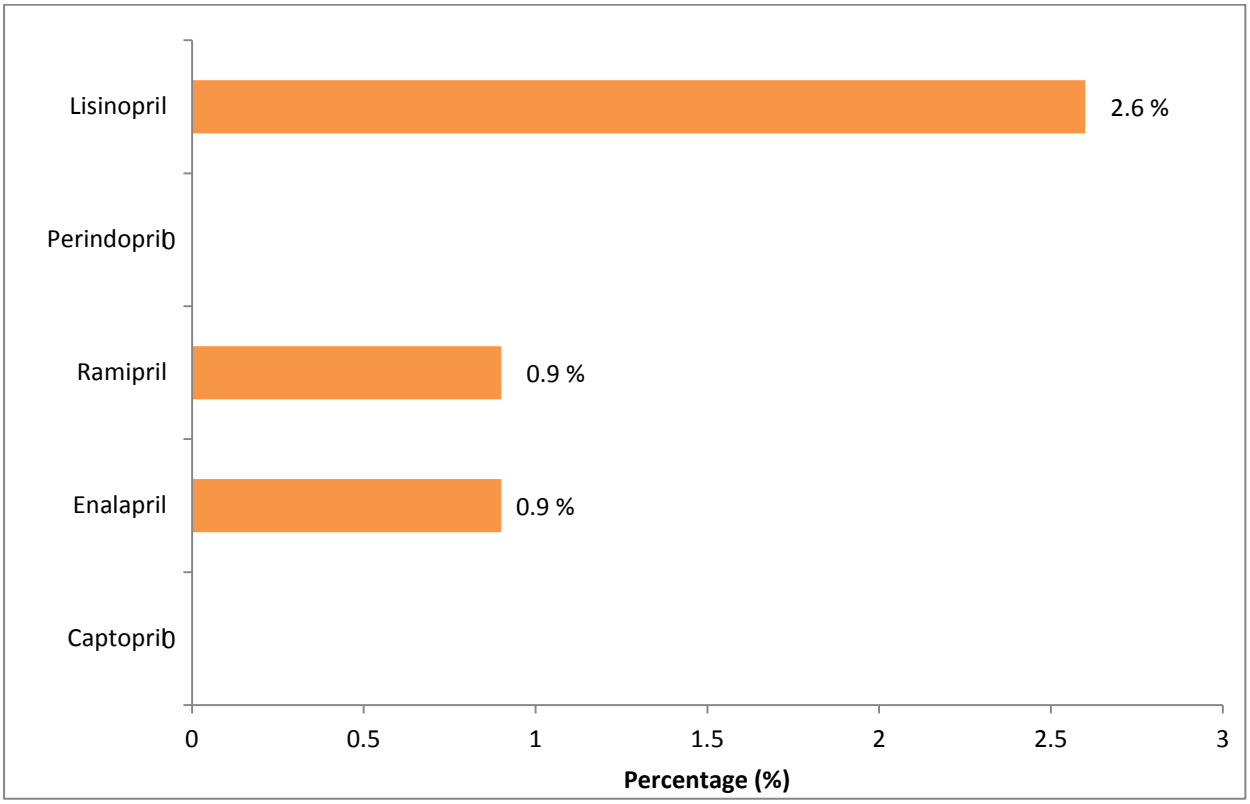
8.17. PREVALENCE OF LIVER DISEASES IN HYPERTENSIVE PATIENTS ON ACE INHIBITORS

Among 5 patients with prevalence of Liver diseases with ACE inhibitors, 0.9% (1) prescribed with Enalapril, 0.9% (1) with Ramipril, 2.6% (3) with Lisinopril. (Table 17, Figure 17)

Table 17. Prevalence of liver diseases in patients on ACE inhibitors (n=112)

S. No.	ACE Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage (%)
1	Captopril	50mg	TD	0	0 %
2	Enalapril	10mg	OD	1	0.9%
3	Ramipril	1.25mg	OD	1	0.9%
		2.5 mg		0	0%
4	Perindopril	20mg	OD	0	0%
5	Lisinopril	40mg	OD	3	2.6%

Figure 17. Prevalence of liver diseases in patients on ACE inhibitors (n=112)



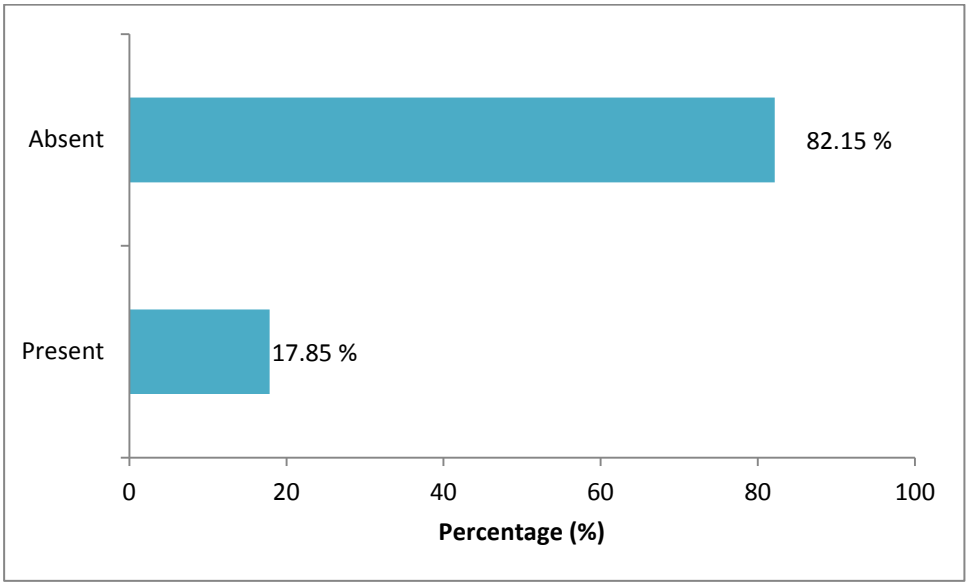
8.18. ASSESSMENT OF PREVALENCE OF HYPERURICAEMIA

Among 112 patients prevalence of hyperuricaemia was present in 20. (Table 18 Figure 18)

Table 18. Prevalence of Hyperuricaemia

Hyperuricaemia	No. of patients with prevalence	Percentage (%)
Present	20	17.85 %
Absent	92	82.15 %

Figure 18. Prevalence of hyperuricaemia



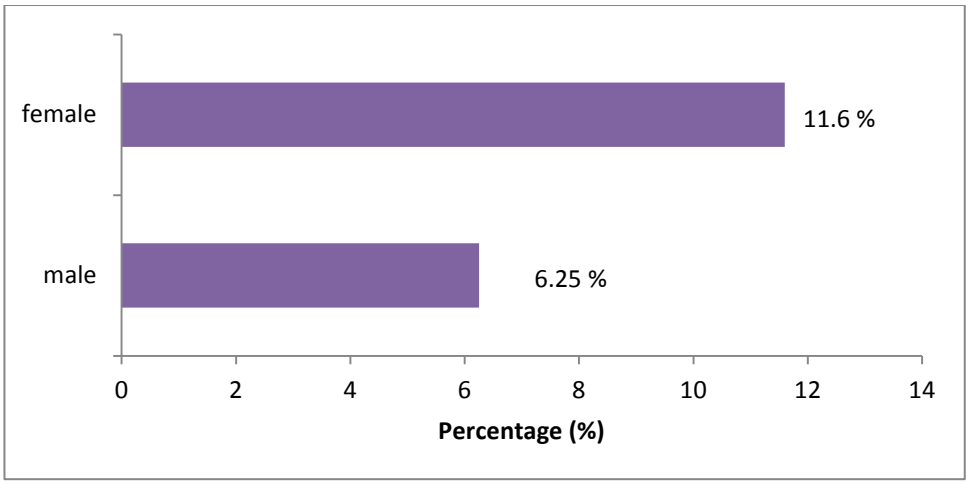
8.19. PREVALENCE OF HYPERURICAEMIA BASED ON GENDER

Among 20 patients having prevalence of hyperuricaemia, 6.25% (7) are male and 11.6% (13) are female. (Table 19, Figure 19)

Table 19. Prevalence of hyperuricaemia based on gender (n=112)

Gender	No. of patients with prevalence	Percentage (%)
Male	7	6.25 %
Female	13	11.6%

Figure 19. Prevalence of hyperuricaemia based on gender (n=112)



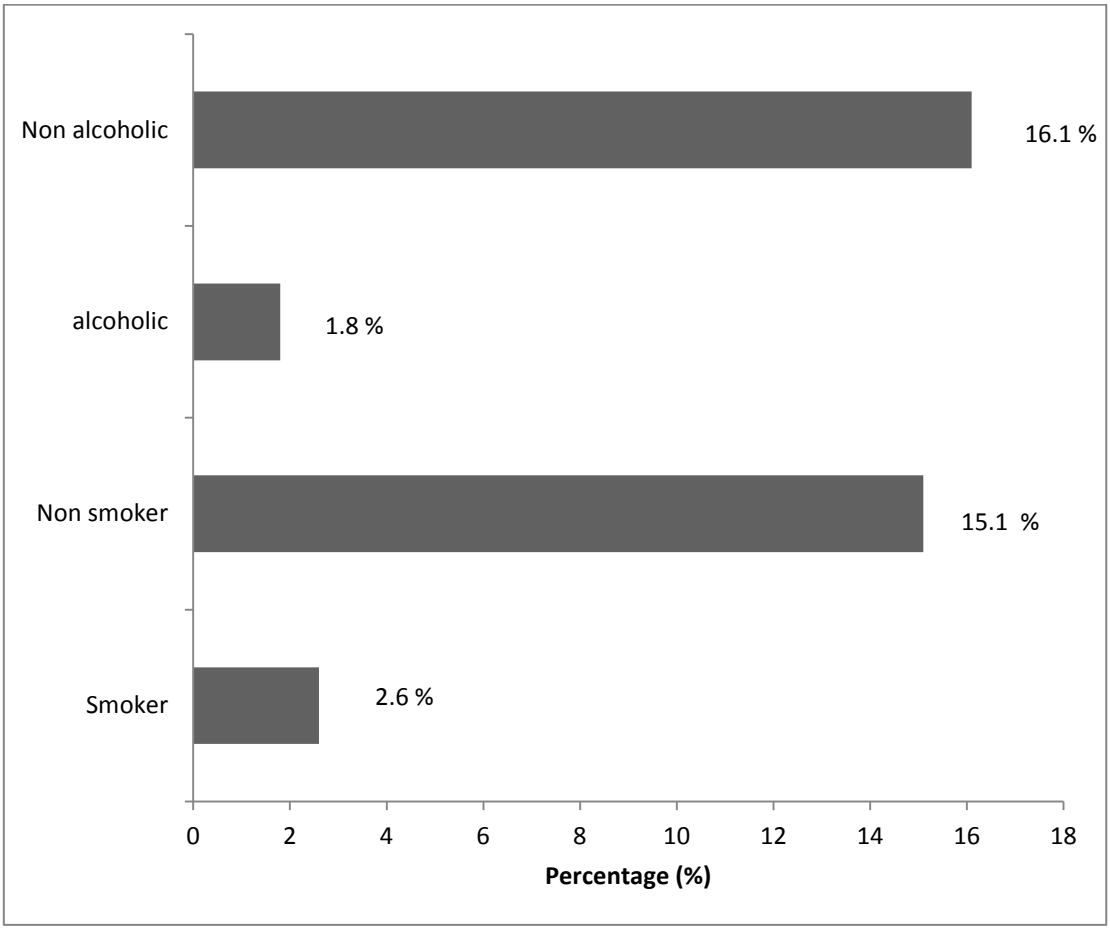
8.20. PREVALENCE OF HYPERURICAEMIA BASED ON SOCIAL HISTORY

Out of 20 patients having prevalence of hyperuricaemia 2.6% (3) are smokers and 15.1% (17) are non smokers, 1.8 % (2) are alcoholic and 16.1 % (18) are non alcoholic. (Table 20, Figure 20)

Table 20. Prevalence of hyperuricaemia based on social history (n=112)

Social history	No. of patients with prevalence	Percentage (%)
Smoker	3	2.6 %
Non smoker	17	15.1%
alcoholic	2	1.8%
Non alcoholic	18	16.1%

Figure 20. Prevalence of hyperuricaemia based on social history (n=112)



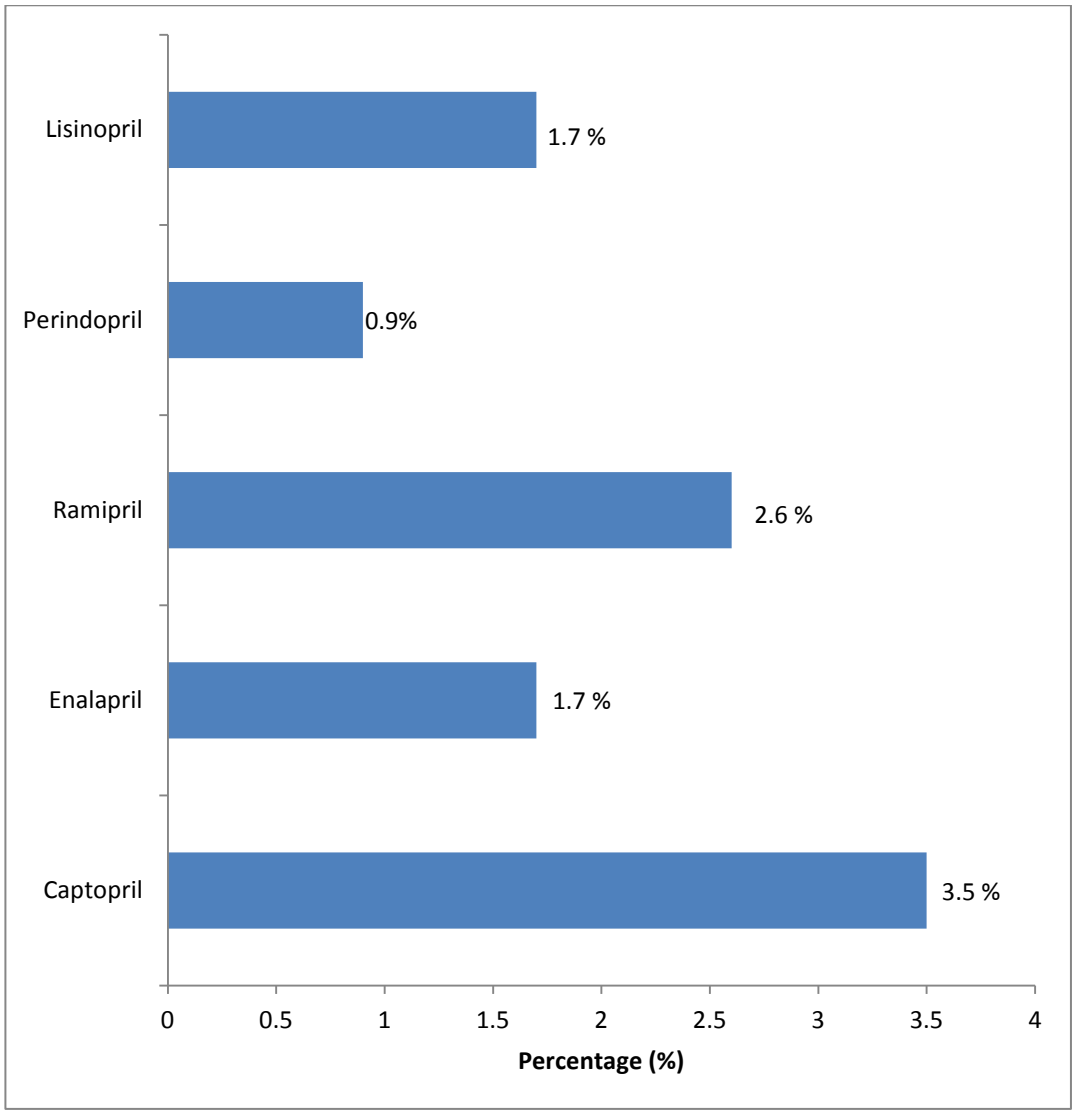
8.21 PREVALENCE OF HYPERURICAEMIA IN PATIENTS ON ACE INHIBITORS

Out of 20 patients with prevalence of Hyperuricaemia on ACE inhibitors, 3.5% (4) prescribed with Captopril, 1.7% (2) prescribed with Enalapril, 2.6% (3) with Ramipril, 0.9% (1) with Perindopril. 1.7 %(2) with Lisinopril. (Table 21, Figure 21)

Table 21. Prevalence of Hyperuricaemia in patients on ACE Inhibitors (n=112)

S. no.	ACE Inhibitors prescribed	Dose	Frequency	Number of Patients	Percentage (%)
1	Captopril	50mg	TD	4	3.5%
2	Enalapril	10mg	OD	2	1.7%
3	Ramipril	1.25mg	OD	1	0.9%
		2.5 mg		2	1.7%
4	Perindopril	20mg	OD	1	0.9%
5	Lisinopril	40mg	OD	2	1.7%

Figure 21. Prevalence of Hyperuricaemia in patients on ACE Inhibitors



9. DISCUSSION

Hypertension is a leading risk factor affecting mortality and disability-adjusted life years worldwide.[55] It is considered to be the third major cause of disease burden, globally.[57] Regardless of the advancement in medical science, reports have shown a rising trend in hypertension prevalence among Indians.[58,59]

It is a chronic disorder, so long term intake of medicine is necessary to control elevated blood pressure. Long term usage of drugs may have adverse impacts on patients health and quality of life.

This study specifically tried to find out the Incidence of Cardiac Events and Prevalence of Hyperuricaemia and Liver Diseases in Hypertensive Patients on ACE Inhibitors.

The total outcome of the study was clear and demonstrative. This study comprised of 112 patients, out of which, most patients were in the age group of 50-59 years Mean age of the study population was 55.7 ± 6years. In this study, the male patients 61% were more predominant in number than the female patients 39%. A study conducted by Aslam et al. showed the patients were in the age group of 50-59 years with regard to gender distribution, 59.7% were males.[24]

A study conducted by Hallberg p et al. shows that most of the patients were having normal body mass index. In present study majority of the patients were overweight.[2]

Out of 112 patients, non smokers and non alcoholic were more exposed to drug related outcomes than smokers and alcoholics.

A total of 112 patients, 51.07% (59) were having 1year duration of Hypertension, 12.1% (13) were having 2-4years duration of Hypertension, 18.01% (20) were having 5-10 years duration of hypertension, and 18.01% (20) were having 10-15 years duration of Hypertension. (Table 6, Figure 6).

The co-morbidities like diabetes mellitus and other complications co-exist with hypertension. But patients with no co-morbidity other than hypertension are more predominant in my study. (Table 7, figure 7)

A total of 112 patients, 6.6% (7) prescribed with captopril, 20.53% (23) prescribed with enalapril, 54.46% prescribed with ramipril, 12.5% prescribed with (14) prescribed with Perindopril and 6.25% (7) prescribed with Lisinopril. (Table 8, Figure 8) This shows that ramipril is the most prescribed drug in the study population.

Incidence of Cardiac Events

The incidence of cardiac events in hypertensive patients with ACE inhibitors were found to be 20.53% which is supporting the study results of Bo Haberg et al which were 27.9% respectively. Our study also shows that the incidence of Angina pectoris and Myocardial infarction were predominant among cardiac events which were 10.71 % and 9.8% respectively. Males were more prone to the incidences of Angina and myocardial infarction. The drugs which cause maximum number in incidences of cardiac events were Ramipril 6%.

Prevalence of Liver diseases

Among 112 patients prevalence of liver diseases due to ACE inhibitors were 5 in which 2.6% (3) had jaundice and 1.7% (2) had hepatitis. (Table 14, Figure 14)

In our study Social history shows among 5 patients having prevalence of liver diseases 1.7% (2) are smokers and 2.6% (3) are non smokers, 3.5% (4) were alcoholic and 0.9% (1) is non alcoholic which clearly demonstrates alcoholics are more prone to incidences of liver diseases. (Table 16, Figure 16)

Among 5 patients having prevalence of liver diseases, 4 were male and 1 was female. (Table 15, Figure 15). Out of 5 patients, prevalence of Liver diseases with ACE inhibitors Lisinopril shows more incidences. (Table 17, Figure 17)

Prevalence of Hyperuricaemia

In our study we observed that 17.85% of patients with hypertension had hyperuricaemia which is in line with the study of Assob et al*,* his study showed that 33% of total population had a high (UA) concentration, with 49.5% being hypertensive.

Our study results also show that females are more prone to hyperuricaemia than male patients with hypertension. (Table 19, Figure 19)

Out of 20 patients having prevalence of hyperuricaemia 2.6% (3 patients) are smokers and 15.1% (17) are non smokers, 1.8 % (2) were alcoholic and 16.1 % (18 patients) were non alcoholic which clearly demonstrates that the subjects with incidences were non smokers and non alcoholics. (Table 20, Figure 20)

In our study, 20 patients with prevalence of Hyperuricaemia due to ACE inhibitors 3.5% (4) prescribed with Captopril, 1.7% (2 patients) prescribed with Enalapril, 2.6% (3) with Ramipril, 60.7%, 0.9% (1) with Perindopril. 1.7% (2) with Lisinopril. This shows captopril shows higher incidences of hyperuricaemia. (Table 21, Figure 21)

10. CONCLUSION

The incidence of Cardiac events like Angina pectoris and myocardial infarction in males were much higher than in females. This indicates that hospitalization of cardiac events for males has increased who were in the age group of 50-59.

Patients who are overweight according to BMI are having the highest risk of cardiac events. Moderate exercises can be recommended to the patients so that the incidence of cardiac events can be possibly reduced.

Patients prescribed with ramipril are having higher incidence of cardiac events among all the ACE inhibitors prescribed. So the pharmacist should actively participate and intervene to reduce the incidences and recommend alternate drug therapy to the physician with aid of evidence based literatures.

The prevalence of liver diseases and hyperuricaemia were low when compared to that of incidences in cardiac events.

The prevalence of liver diseases like jaundice and hepatitis were more in male population and also predominant with alcoholics .The drug Lisinopril shows more incidences when compared to other ACE inhibitors so alternative therapy along with effective dosage regimen should be recommended.

The prevalence of hyperuricaemia in patients with ACE inhibitors was higher with females.BMI profile of the patients also has considerable effect over the prevalence of

hyperuricaemia and the drug captopril causes higher number of incidences of hyperuricaemia.

As per the findings, Incidences of Drug induced problems are common in a hospital and some of them results in increased healthcare cost due to the need of intervention and increased length of hospital stay. Early identification and early initiation and early recovery help to avoid complications hence knowledge about the drug related outcomes are essential to avoid drug related problems. Active involvement of well trained clinical pharmacist for assessing the incidences and prevalence and creating awareness in health care professionals and patients, regarding to need of reporting the incidence could improve the scenario under reported hospital.

In present study we have documented the incidences and prevalence of drug related outcomes in hypertensive patients with ACE inhibitors thereby increasing awareness among health care professionals.

11. LIMITATIONS

- Most of the incidences were left unreported which may be attributed to the lack of awareness among nurses and attitude of health care professionals.
- Limitation of sample size.
- Incidence rate obtained of ADRs in Patient setting represents a skewed image of the true incidence, which is often difficult to estimate.

12. FUTURE OUTLOOK

- To strengthen reporting of incidences and prevalence of drug related outcomes in patients, nurses, physician and other health care professionals by improving awareness and education program in hospital.
- To extend the project to a large population in community settings by providing training to working community pharmacist's to encourage them in reporting and monitoring of incidences.
- To assess the risk factors associated with the incidences.

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Website : www.vivekanandha.ac.in email : vivekanandhamedicalcare@gmail.com

Healing Touch with Mother's Care

Ref. No.: SVCP/IEC/JAN/2016/13

Date: 23.07.2016

To

R. Nithya,
M-Pharm. (Pharmacy Practice) Student,
Swamy Vivekanandha College of Pharmacy,
Elayampalayam, Tiruchengode – 637205.

Sub: Approval of the Study Protocol- Reg

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "AN INVESTIGATION ON THE INCIDENCE AND PREVALENCE OF DRUG RELATED OUTCOMES IN HYPERTENSIVE PATIENTS ON ACE INHIBITORS" under the guidance of Mr. Joseph Stalin D on 15.07.2016.

The following documents were reviewed:

a. Study protocol
b. Patient Information Sheet/ Informed Consent Form
c. Study data collection form
d. Principal Investigator's/ Co-PI current CV.
e. Investigator's undertaking

The following members of the ethics committee were present in the meeting at Vivekananadha Medical Care Hospital.

1. Dr. Sathish K M - Chairman
2. Dr. Palanisamy A - Member Secretary
3. Dr. Poovendran T - Member
4. Dr. Ananda Thangadurai S - Member
5. Dr. Vinoth Prabhu V - Member

We approve the study to be conducted in its presented form.

The Institutional Ethics Committee to be informed about the progress of the study, any serious adverse events occurring in the course of the study, any changes in the protocol and patient information/informed consent and to provide a copy of the final report on completion.

23/7/16.

Dr. A. Palanisamy,

MEMBER SECRETARY,
Institutional Ethics Committee,
VIVEKANANDHA MEDICAL CARE HOSPITAL,
ELAYAMPALAYAM-637 205,
Tiruchengode Tk., Namakkal Dt., T.N.

Swamy Vivekanandha College of Pharmacy, Elayampalayam

Institutional Ethics Committee

INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(Strike off items that are not applicable)

I / We (write name of the investigator(s) here), am / are carrying out a study on the topic: as part of my / our research project being carried out under the aegis of the Department of:

(*Applicable to students only*): My / our research guide is:

The justification for this study is:

The objectives of this study are:

Primary Objective:

Secondary Objective:

Sample size:

Study volunteers / participants are (specify population group & age group):

Location:

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration):

Data collected will be stored for a period of years. We will / will not use the data as part of another study.

Health education sessions: Number of sessions: 1.Approximate **duration** of each session:

Clinical examination (Specify details and purpose):

Blood sample collection: Specify quantity of blood being drawn: No. of times it will be collected:

Whether blood sample collection is part of routine procedure or for research (study) purpose:

1. Routine procedure 2. Research purpose

Specify **purpose**, discomfort likely to be felt and side effects, if any:

Whether blood sample collected will be stored after study period: Yes / No, it will be destroyed

Whether blood sample collected will be sold: Yes / No

Whether blood sample collected will be shared with persons from another institution: Yes / No

Medication given, if any, duration, side effects, purpose, benefits:

Whether medication given is part of routine procedure: Yes / No (If not, state reasons for giving this medication)

Whether alternatives are available for medication given: Yes / No (If not, state reasons for giving this particular medication)

Final interview (specify approximate duration): NA If **photograph** is taken, purpose:

Benefits from this study**:**

Risks involved by participating in this study:

How the **results** will be used:

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Xg;Gjy; gbtk;

Njjp:

---------- Mfpa ehd;> VMCH kUj;Jtkidapy; ---------- Jiwapd; fPo;> ----------vd;w jiyg;gpy; Ma;T Nkw;nfhs;s cs;Nsd;.

vd; Ma;T topfhl;b:

Ma;T Nkw;nfhs;tjw;fhd mbg;gil:

Ma;tpd; Nehf;fk;:

Ma;T Nkw;nfhs;Sk; ,lk;:

Ma;tpd; gyd;fs;:

,e;j Ma;tpy; fpilf;Fk; jfty;fs; ---------- tUlq;fs; ghJfhf;fg;gLk;. ,it NtW ve;j Ma;tpw;Fk; gad;gLj;jg; gl khl;lhJ. ve;j epiyapYk; cq;fisg; gw;wpa jfty;fs; ahUf;Fk; njhptpf;fg;gl khl;lhJ. mit ,ufrpakhf itf;fg;gLk;.

,e;j Ma;tpy; gq;Nfw;f xg;Gf;nfhs;Stjhy; ve;j tpjkhd gyDk; cq;fSf;Ff; fpilf;fhJ. ve;j Neuj;jpy; Ntz;LkhdhYk; Ma;tpypUe;J tpyfpf; nfhs;Sk; chpik cq;fSf;F cz;L.

Ma;tpypUe;J tpyfpf;nfhs;tjhy; cq;fSf;F mspf;fg;gLk; rpfpr;irapy; ve;j tpj khw;wKk; ,Uf;fhJ.

,e;j Muha;r;rpf;fhf cq;fsplk; rpy Nfs;tpfs; Nfl;fg;gLk; / rpy ,uj;j khjphpfs; my;yJ jpR khjphpfs; vLf;fg;gLk;.

NkYk;> ,e;j Ma;tpy; gq;F nfhs;tJ cq;fs; nrhe;j tpUg;gk;. ,jpy; ve;j tpjf; fl;lhaKk; ,y;iy. ePq;fs; tpUg;gg;gl;lhy;> ,e;j Ma;tpd; KbTfs; cq;fSf;Fj; njhpag;gLj;jg;gLk;.

Ma;thshpd; ifnahg;gk; :

Njjp :

Ma;Tf;Fl;gLgthpd; xg;Gjy;:

ehd; ,e;j Muha;r;rpapd; Nehf;fk; kw;Wk; mjd; gad;ghl;bidg; gw;wp njspthfTk;> tpsf;fkhfTk; njhpag;gLj;jg; gl;Ls;Nsd;. ,e;j Muha;r;rpapy; gq;F nfhs;sTk;> ,e;j Muha;r;rpapd; kUj;Jt uPjpahd Fwpg;Gfis tUk; fhyj;jpYk; cgNahfg;gLj;jpf; nfhs;sTk; KO kdJld; rk;kjpf;fpNwd;.

Ma;Tf;Fl;gLgthpd; ngah;> Kfthp :

ifnahg;gk; :

Njjp :

DATA ENTRY FORM

NAME OF PATIENT:				IP NO.	DEPARTMENT	DOA	DOD
AGE/SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	FAMILY HISTORY:			OCCUPATION
COMPLAINTS ON ADMISSION:							
MEDICAL HISTORY:				MEDICATION HISTORY:			
SOCIAL HISTORY				KNOWN ALLERGIES:			
ALCOHOLIC	SMOKER	TOBACCO	OTHERS				

VITAL SIGNS (PROGRESS CHART)

PARAMETERS	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9	DAY 10
BP(mmHg)										
Temp										
PR(beats/min)										
RR(breaths/min)										

BLOOD SUGAR	**ELECTROLYTES**	
FBS(70-110 mgs/dl)	SODIUM(135-145 mmol/l)	CALCIUM(0.8-2.0 mmol/l)
PPS(80-140 mgs/dl)	POTASSIUM(3.5-5.1mmol/l)	BICARABONATES
RBS(70-170 gm/dl)	CHLORIDE(97-106 mmol/l)	

HAEMATOLOGY

Sl.No.	Parameters	Patient value	Normal value
1.	Hb		F: 11-16 gms/dl M: 11.5-18 gms/dl
2.	RBC'S COUNT		4.0-6.0 million/cu.mm
3.	HCT		35-60%
4.	MCV		80-100 cu.micron
5.	MCH		27-31 pg
6.	MCHC		33-37%
7.	RDW		11.6-13.7 %
8.	MPV		7.8-11 cu.micron
9.	WBC'S COUNT		4500-10500 cells/cu.mm
10.	ESR		M:< 10 F:< 20
11.	CLOTTING TIME		5-10 min
12.	BLEEDING TIME		1-6 min
13.	PROTHROMBIN TIME		
14.	PLT		1.5-4.5 lakhs/cu.mm
15.	PLATELETCRIT		0.17-0.35 %
16.	PDW		9-4 cu.micron
DIFFERENTIAL LEUKOCYTE COUNT			
17.	POLYMORPHS		42-75 %
18.	LYMPHOCYTES		21-51 %
19.	EOSINOPHILS		1-6 %
20.	MONOCYTES		1-4 %

LIVER FUNCTION TEST		
TOTAL BILIRUBIN (0.4-1 mg/dl):	S.TOTALCHOLESTEROL(<240mgs/dl):	SGOT(0-40Iu/l):
DIRECT BILIRUBIN (0.1-0.4 mg/dl):	S.TRIGLYCERIDE (70-170mgs/dl):	SGPT(0-65 Iu/l):
INDIRECT BILIRUBIN (0.2-0.8 mg/dl):	S.HDL(40-60mgs/dl):	GGTP(11-45Iu/l):
TOTAL PROTEIN (6-8 gms/dl):	S.LDL(0-140mgs/dl):	ALKP(0-258Iu/l):
ALBUMIN (3.5-5.5 gms/dl):	S.VLDL(0-38mgs/dl):	GLOBULIN (2-3.5 gms/dl):

RENAL FUNCTION TEST	Patient value	Normal range
S.UREA		20-40 mgs/dl
URIC ACID		2.3-6.1 mg/dl
S.CREATININE		0.6-1.40 mgs/dl

URINE EXAMINATION		
COLOUR	SUGAR	RBC
TRANSPARENCY	ALBUMIN	PUS CELLS
REACTION	OCCULT BLOOD	EPI. CELLS
SPECIFIC GRAVITY	KETONE BODY	CAST & CRYSTALS
BILE SALTS & BILE PIGMENTS	WBC	BACTERIA

IMAGING STUDY REPORT

OTHER INVESTIGATION:

DIAGNOSIS

TREATMENT CHART

SL. NO	DRUG NAME	DOSE	FREQ	ROA	DAYS OF DRUG ADMINISTRATION						
					D1	D2	D3	D4	D5	D6	D7
1											
2											

3											
4											
5											
6											
7											
8											
9											
10											

DRUG INTERACTION/ADVERSE DRUG REACTIONS

DRUGS	EFFECTS	INFERENCE

DISCHARGE MEDICATION

	DRUGS		**DOSE**	**FREQ**	**DURATION OF THERAPHY**
	T.Name	**G.Name**			
1					
2					
3					
4					
5					
7					
8					
9					
10					

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Certificate

OF PARTICIPATION

This Certificate is awarded to

Dr/Mr/Ms/Mrs R. NITHYA

has participated in a National level seminar on "Clinical Pharmacy Practices in India – Current Scenario" on 31-08-2017

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Certificate of Participation

This is to certify that Dr. / Ms. / Mrs. / Mr. / NITHYA . R *has participated as Undergraduate / Postgraduate / Faculty in the Conference on "Clinical Implication for Paramedics" conducted by the College of Allied Health Sciences on 24th June 2017, at Vivekanandha Auditorium, Elayampalayam, Tiruchengode - 637 205. The education activity has been awarded* **10 Credit** *points by The Tamil Nadu Dr. M.G.R. Medical University.*

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Vivekanandha Medical Care Hospital ALLIED HEALTH SCIENCE Tiruchengode

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Tamilnadu.

National Level Seminar on

"CLINICAL PHARMA PRACTICE - INDIAN AND GLOBAL SCENARIO" (CPP-IGS 2017)

CERTIFICATE

This is to certify that Mr./Ms./Prof./Dr. ....NITHYA R..... has participated as delegate in the National Level Seminar **"CLINICAL PHARMA PRACTICE - INDIAN AND GLOBAL SCENARIO"** (CPP-IGS 2017) on 11th August - 2017, organized by **Department of Pharmacy Practice,** Sponsored by **The Tamilnadu Dr. M.G.R Medical University,** Chennai.

Dr. T. TAMILSELVAN
Organizing Secretary

Dr. G. MURUGANANTHAN
Convener

Prof. Dr. M. KARUNANITHI
Chairman & Secretary